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KAROLINSKA INSTITUTET
IN COMMEMORATION
OF THE 150TH ANNIVERSARY

Although Karolinska Institutet will be known to many as the authority electing the individual to be awarded the Nobel Prize in Medicine, there must be relatively few outside the Scandinavian countries who possess any great knowledge of its history or activity. This year the institute celebrates the 150th anniversary of its foundation and in commemoration of this occasion the following short presentation of the institute is offered to the readers of Acta Radiologica. The present issue is also published in honour of the institute as all the articles emanate from members of the medical profession attached to Karolinska Institutet who work in the fields covered by our periodical.

The inception of the institute was brought about by the war of 1808—1809 between Sweden and Russia. It was found that the deaths of soldiers at that time were caused not so much by the bullets of the enemy as by epidemic diseases, traumatic fever and scurvy. The authorities responsible for the care of the sick realized their former neglect and with a view to remedying the recognized shortcomings founded the institute with the objective of giving instruction to and providing training for army surgeons. The full name given to the foundation was 'Kungl. Karolinska Medico-Kirurgiska Institutet'. There were two professors at this newly founded medical college who soon won universal fame, the chemist Jöns Jacob BERZELIUS and the anatomist Anders RETZIUS. From its initiation and for many years to come the mission of the institute was to foster surgeons and give complementary instruction in

military medicine and practical medical care to doctors of medicine wh had graduated from the two Swedish universities (Upsala and Lund). It al very soon became the aim of the professors of the institute to obtain full equali with the two universities but it was not until the year 1874 that the institu was authorized to examine the undergraduates in subjects embracing th elements of basic medical training and to confer the degree of 'candidate' f medicine (approximately corresponding to the English degree of bachelor f medicine), and not until 1906 to confer the degree of doctor of medicine.

The institute had however as early as in the 19th century developed into a progressive and important medical centre. It became an established rule th t new medical specialities in theoretical medical research as well as in exper - mental and clinical medicine should be represented at Karolinska Institut t before the corresponding faculties were founded at our universities. Kar - linska Institutet has therefore in Sweden been a precursor in promoti g advancements in medical science. In the theoretical field it was even the fir t medical college in the world to possess a professorial chair in medical chem - istry, the one occupied by BERZELIUS. As far back as 1813 instruction in pharmacology had been entrusted to a professor, and in 1874 the institute appointed its first professor in physiology. Histology became a special subject of instruction in 1877, when it was separated from the branch of anatomy, and the first professorial chair in histology was occupied by Gustaf RETZIUS who had become recognized for his investigations on the nervous system.

Progress has been very rapid during the present century, and in particular during the past two decades when new branches of medicine have developed and special departments for new specialities have been established at the in - stitute. There are now two professorial chairs in pathology. The chair in neurophysiology was established in 1950, while a second chair in physiology was founded in 1948. Another chair in chemistry was obtained in 1947. A research professorship in medical cytology was created in 1944, and one in medical physics in 1951. The subjects of bacteriology and virology had to a certain extent been neglected, and it was not until 1946 and 1948, respectively, that professorial chairs for these specialities were obtained. The professorial chair in biochemistry, to which Hugo THEORELL had been nominated in 1937, was in 1959 transferred to Karolinska Institutet. A professorial chair in tumour biology was founded in 1957 and in the same year one in theoretical research on alcoholism.

Since the beginning of the 19th century Serafimerlasarettet has been the hospital and affiliated medical school of Karolinska Institutet and it was at this hospital that the courses of instruction in surgery and the practice of medicine were given. Both surgery and medicine became represented at an early stage by two clinics. The two medical clinics were located at Serafimerlasarettet, while one of the surgical clinics was opened in 1923 at a city hospital, Mar Sjukhus, where it remained until 1940, the year of inauguration of Karolinsk

sj huset. Among the professors in medicine in recent years who were well kn wn may be mentioned the late H. C. JACOBAEUS. Oto-rhinolaryngology w s in 1912 detached from general surgery and obtained its own department. P stic surgery developed in the decade of 1930 as a new speciality for Sweden a l a separate clinic was obtained in 1944. Anaesthesiology was a subjeect th t had long been neglected despite the fact that Professor John BERG, the su geon, had already as early as 1898 stressed the necessity of providing tr ning for specialists in this branch; it was not until 1949 that a separate d partment was obtained. Pediatric surgery already in 1876 had its own cl ic, and a second clinic was created in 1952. Cardiac and thorax surgery ha made rapid progress at the institute, and a professorial chair in thoracic su gery was created in 1948. A department of experimental surgery is attached to this clinic.

Disorders of the nervous system have been objectives of intense research at the institute with investigations conducted both at the neurologic and neurosurgical clinics as well as at the roentgen department. The professorial chair in neurology was founded in 1885. The scientific activity of the institute in this field was earlier concentrated primarily on investigating the anatomical and pathologic conditions while nowadays it is more directed towards the physiologic aspects of the neurologic conditions. A professorial chair in neurosurgery was created in 1935 for Herbert OLIVECRONA. A faculty for the combined subjects of obstetrics and gynecology had been constituted in 1864, and a second was established in 1878. Ophthalmiatrics became represented with a professorial chair in 1880. Children's diseases had its first professor in 1845, and a second professorship in pediatric medicine was obtained later. The care of the disabled in Sweden had been well organized already at the beginning of this century by the professor of orthopedics at that time. The institute has naturally also a chair in psychiatrics, for which subject there are now, from this year, two chairs. Medico-legal psychiatrics became represented in 1920. Dermatovenerology is of course represented, and allergology as well.

This brief survey of the more important faculties represented at Karolinska Institutet is of necessity not complete. There are a number of other specialities which have not been mentioned, such as endocrinology, urology, and pediatric pathology, for which there are special departments with assistant professors as directors. The outline given may, it is hoped, convey a general idea of the expansion and purpose of the institute and serve as a background against which the development in the field of medical radiology may be presented.

It was the professor in surgery who in 1904 took the initiative of starting a combined diagnostic and therapeutic roentgen laboratory at Serafimerlasarettet, the direction of which in 1906 was entrusted to Gösta FORSSELL, the man whose genius and creative powers in all essentials guided the development of medical radiology in Sweden.

The progress was rapid. Fritiof LENNMALM, the Dean of Karolinska Institutet,

made in 1910 the following statement: "Not many years have elapsed since Röntgen made his discovery, and medical roentgenology has already grown to such an extent and gained such widespread importance in all branches of medicine that it is now firmly established as an indispensable scientific branch. A man must be busy if he is to master the whole subject of radiology." The leading idea of Gösta FORSSELL was that roentgenology should be represented by a physician who made it his sole occupation. Only in this way could achievements in the right direction be expected and rapid scientific progress made possible, to ensure radiology being adequately incorporated as a special branch of knowledge, to the general benefit of medical practice. In order to provide a basis for such accomplishments it would, according to Gösta FORSSELL, be necessary to have a central roentgen department in every hospital and to ensure that an independent position was secured for the radiologists, in the same manner as for the directors of other departments. These ideas have been appreciated and accepted by the Swedish medical authorities; it may be recalled that in this respect the conditions in Sweden differ from those in many other countries. The fact that medical radiology in Sweden has gained a widespread reputation for being of the highest international standard is probably largely a result of the conceptions of Gösta FORSSELL which were embraced and realized at Karolinska Institutet.

In place of the old laboratory, a new central roentgen department, designed and planned by Gösta FORSSELL, was established in 1911 at Serafimerlasarettet. This department was well ahead of time. It consisted of two diagnostic laboratories and one therapeutic laboratory, each with a separate, protected room in which the roentgen equipment was operated. It may also be mentioned that in Sweden attention was already at this time directed to the importance of providing adequate means of radiation protection. This is probably one of the reasons why in Sweden we have been spared such radiation damage as has often occurred in other countries during the childhood of radiology. Separate ray-proof control rooms have not as yet been effectively introduced in all countries.

FORSSELL at first gave instruction to volunteer students at the institute, but from 1917, when he was nominated professor in medical radiology, the instruction became more firmly organized and the courses compulsory. In 1936 the subject of medical radiology was divided into two branches and two professorial chairs were established, one in roentgen diagnostics, which was retained by FORSSELL, and one in radiotherapy for which Elis BERVEN was nominated the first professor. Facilities for giving roentgen and radium treatment existed at Serafimerlasarettet but in 1910 another centre, Radiumhemmet, was founded. This centre is exclusively devoted to radiation therapy. FORSSELL was active as director also here until BERVEN in connection with his nomination to professor assumed the leadership. Karolinska Institutet in 1936 had consequently succeeded in fullfilling the hopes expressed by FORSSELL in his opening

lecture at the Fifth International Congress of Radiology: "A complete divorce between roentgen diagnostics and radiotherapy confers such great advantages both for research work and instruction, as well as for the utilization of radiology in medical practice, that I consider one of radiology's highest hopes to be the division, as soon as possible, of the radiological work, at university and other large hospitals, in order to embrace separate and independent roentgen diagnostic and therapeutic departments."

As a result of the expanding activity of the theoretical departments as well as the clinics of Karolinska Institutet at Serafimerlasarettet these gradually became more and more unsatisfactory. During the third decade of this century, after considerable investigative work and prolonged planning, new buildings were erected at the city border between Stockholm and Solna. There are now twenty-five theoretical institutions located on a separate piece of ground and, further, some thirty clinics incorporated with Karolinska Sjukhuset situated close by.

Radiumhemmet in 1937 was the first of the clinics belonging to Karolinska Sjukhuset to come into use. Two research departments were established in connection with it, one for radiopathology and one for radiophysics, each with a professor as director. Later, a separate research department for radiobiology and a department for experimental tumour research were instituted. There is a large central roentgen department in the central building of Karolinska Sjukhuset directed by a professor in roentgen diagnostics. Pediatric medicine with its own roentgen department under the direction of a pediatric radiologist is housed in a separate building. The Thorax Clinic is contained in a building comprising a medical clinic for lung diseases, a clinic for pulmonary and cardiac surgery, as well as a roentgen department under the direction of a specialist radiologist. In about three years time the neurologic and neurosurgical departments, which still remain at Serafimerlasarettet, are to be transferred to a new building containing various departments for neurologic diseases and located on the site reserved for the institutions of the expanding Karolinska Sjukhuset. The present professorial chair in roentgen diagnostics combined with neuroradiology, held at the roentgen department of Serafimerlasarettet, will then be divided. The neuroradiologic activities will be concentrated in a special roentgen department housed in the institute's new building for neurologic diseases. Fifty years have now elapsed since LENNMALM made his statement that a man must specialize in radiology in order to master the subject. The progress at Karolinska Institutet in the field of medical radiology has since then been so rapid that first a subdivision into roentgen diagnostics (represented by two professorial chairs) and roentgen therapy was found necessary and that now the need for a similar subdivision of roentgen diagnostics as in surgery is beginning to be felt. Thus three subspecialities in roentgen diagnostics have developed: pediatric roentgen diagnosis, thorax diagnosis and neuroradiology. With regard to the radiologic specialities, the theoretical and experimental

as well as those in the service of clinical medicine, there is no other medic l college which can show a similar expansion and differentiation as Karolinsl a Institutet.

Karolinska Institutet is a large organization and its specialization in scientif c research and in the practice of medicine is well advanced. It is evident therefo e that the present survey can only impart a general and somewhat sketch y picture of the institute as an entity. It is not possible to go into detail as regar s the different aspects of research, or the instruction and routine work pursu d at the various institutions of Karolinska Institutet, but it may be emphasiz d that the institute holds a unique position in the field of medicine in Sweden.

When Alfred Nobel delegated to the institute the task of electing the individu l to be awarded the annual prize for having rendered the greatest service to humanity by making the most important discovery in the fields of physiolo y and medicine during the previous year, the institute was charged with its mo t honourable commission. This however also involved great responsibilities. To accomplish this task it is necessary for the body of members of the institute closely to follow the actual progress of medicine, which in its turn requires an active participation in all the relevant fields of research. In this respect therefore the duty delegated upon the institute has been of the greatest importance for its development. The interest in all aspects of scientific activities has been greatly stimulated and this has also facilitated the application in clinical medicine and medical practice of the results obtained by scientific research.

Acta Radiologica, on the occasion of the celebration of the 150th anniversary of Karolinska Institutet, would like to give expression to the hope that the rapid progress in scientific activity at the institute may continue as before to serve the development of medicine, to the benefit of humanity.

Erik Lindgren

FROM ROENTGENDIAGNOSTIC DEPARTMENT D (DIRECTOR: DOCENT Å. LINDBOM) AND THE INSTITUTE OF RADIOPATHOLOGY (DIRECTOR: PROF. L. SANTESSON), KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

ANGIOGRAPHY IN OSTEOID OSTEOMA

by

Å. LINDBOM, N. LINDVALL, G. SÖDERBERG and H. SPJUT

The roentgenographic appearance of osteoid osteoma has become well known in recent years through the publication of text-books on bone tumors (DAHLIN, JAFFE, LICHTENSTEIN). In typical cases a fairly reliable diagnosis may be made by means of roentgen examination. The difficulty of differentiating osteoid osteoma from a sclerosing osteomyelitis or an intracortical bone abscess has been pointed out by several authors. JAFFE mentions that osteoid osteomas are highly vascular. He believes that there is an association between this hypervascularization and the pain which is the dominating symptom in these cases. We have found that the hypervascularization may be demonstrated by means of angiography and the differential diagnosis between osteomyelitis and osteoid osteoma thus facilitated.

Angiography with a serial technique was performed in two cases of osteoid osteoma of an ulna and a fibula respectively. The lesion of the ulna occurred in a 15-year-old boy and had a typical roentgenographic appearance with marked bony sclerosis around a clearly discernible nidus (Fig.1). The other case, in the proximal fibular metaphysis of a 13-year-old girl, had a more unusual appearance. The nidus was large and superficial and probably located mainly in the periosteum. The proximal end of the fibula was diffusely sclerotic and had a considerably greater diameter than the head of the fibula of the opposite side (Fig. 2).

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a b c

Fig. 1. Osteoid osteoma of ulna. Serial angiography. a) Arteries not yet filled. b) Arterial phase. A feeding artery is seen. The nidus is diffusely filled with contrast medium except for a 1 mm broad peripheral zone, which is still seen also in the venous phase (c).

In both of these cases contrast filling of the nidus was obtained in the course of angiography. The number of vessels surrounding the nidus in the fibula was markedly increased. The osteoid osteoma of the ulna was examined by means of an automatic seriograph and stereoscopic films were obtained. A small feeding artery was clearly seen in the early arterial phase. The density of the nidus increased during the inflow of contrast medium into the lesion and then gradually decreased; in a 1 mm broad zone peripherally in the nidus the density was the same in all the films of the series (Fig. 1). No such difference of contrast filling between the central and peripheral parts could be discerned in the nidus in the fibula.

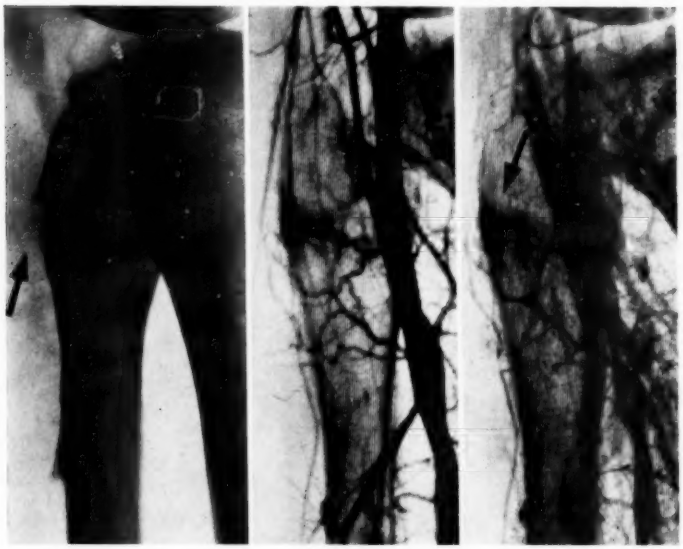
The later course of this second case is of interest. The lesion in the fibula was curetted with resultant relief of symptoms. Two and a half years after the operation the patient complained of slight pain in the same region. Roentgen

a b

Fig. 2. Osteoid osteoma of fibula. a) Superficial large nidus with enlargement of proximal end of bone. b) In the angiogram, hypervascularization of the lesion is seen.

examination demonstrated a small superficial defect in the bone at the same site as the original nidus. At angiography this defect contained highly vascular tissue (Fig. 3). The symptoms were however deemed as unimportant and no operative intervention was performed. At re-examination two and a half years after this the superficial defect in the bone had almost totally disappeared, and the patient was free from symptoms. At this latest examination, five years after the operation, the upper ends of the fibulae were of almost equal size (Fig. 4).

Histologic examination of the vessels was performed in these two osteoid osteomas. Slides from a third case not submitted to angiography were also examined. The degree of vascularity was computed as in an earlier work on the vessels in fibrosarcomas (LAGERGREN et coll.). It was found to be moderately high compared with earlier investigated cases of fibrosarcomas. The vascularity



a b c

Fig. 3. Same case as in fig. 2, two and a half years later. a) Small nidus still visible. b) and c) Angiograms in which intense vascularization of the nidus is seen.

in the tissue of the osteoid osteoma was thus found to be comparable to that of fibrosarcomas of a moderate degree of malignancy. The vessels had however a different, more mature appearance. They were fairly well differentiated. Small arteries and precapillaries were seen but the majority of the vessels in the sections were normal, partly dilated, thin-walled capillaries (Fig. 5); they had a wavy course, their walls generally consisting of only one layer of endothelial cells with a very thin drawn-out cytoplasm with nuclei which bulged into the lumen. The capillaries generally had an inner diameter between ten and thirty microns, but some of them were considerably wider. No bag-shaped dilatation of the vessels as in some malignant tumors could be seen. The histologic investigation thus showed that the tissue in the nidus was hypervascularized to such a degree that the increased density observed during angiography could well be explained.

Angiography was also performed in two cases of sclerosing osteomyelitis, one localized in the proximal metaphysis of a femur and one in the distal femoral metaphysis. The history, the roentgenographic bone changes, and the findings at operation strongly suggested osteoid osteoma in one of these cases. Both patients were treated surgically. The histologic findings of the material from

a b

Fig. 4. Same case as in fig. 2, five years later. Nidus almost totally disappeared. Slight irregularity of cortex, with a small dense area which is possibly the calcified rest of the nidus. Fibular head now only slightly larger than the one of the opposite side (b).

the lesions and the subsequent clinical course conformed with osteomyelitis. No increased vascularity in or around the pathologically changed regions could be seen in these two cases either at angiography or in the microscopic investigation.

Discussion and Conclusions

The nidus of an osteoid osteoma contains considerably more vessels than the surrounding bony and soft tissues. The majority of these vessels are slightly dilated capillaries. When contrast medium during angiography passes through these vessels the nidus becomes diffusely filled with the material. In sclerosing osteomyelitis no increased vascularity could be demonstrated at angiography. Hypervascularization was found in chronic inflammation by LAGERGREN et coll. especially in synovial tissue. An increased vascularity could therefore be expected also in a chronic osteomyelitis. It is, however, unlikely that the vascularity should be increased in the necrotic tissue, such as seen in an abscess. It is therefore suggested that angiography may be a useful method for distinguishing between osteoid osteoma and bone abscess.

Fig. 5. Photomicrograph of osteoid osteoma. Increased vascularity of tumor tissue. Arrows indicate wide capillaries.

JAFFE's view that the osteoid osteoma is a peculiar kind of benign tumor is now generally accepted. Benign tumors (e. g. lipomas, enchondromas) are usually not more vascularized than the surrounding tissue from which the tumor originates. There are however some well known exceptions to this rule, i. e. giant cell tumor and meningeoma. The osteoid osteoma can with regard to vascularity be compared to these neoplasms.

One of our cases of osteoid osteoma presented a small rest of the tumor, probably persisting from the first operation. This small focus could be demonstrated angiographically as a hypervascularized area. Five years after the initial operation the focus had disappeared. This lends support to the concept that osteoid osteomas may disappear spontaneously (VICKERS). The early active phase of this osteoid osteoma was accompanied by a considerable increase of growth in the adjacent portions of the fibula. When the tumor had disappeared the bone regressed to almost normal size.

SUMMARY

The hypervascularization of the nidus of an osteoid osteoma may be demonstrated by means of angiography. The roentgenographic diagnosis may thus be supported and the differentiation from bone abscess facilitated.

ZUSAMMENFASSUNG

Es ist möglich, die Hypervaskularisation des Nidus eines osteoiden Osteoms mittels Angiographie zu demonstrieren. Die Röntgendiagnose wird dadurch gestützt und die Differenzierung gegenüber Knochenabszess erleichtert.

RÉSUMÉ

L'hypervascularisation du nidus d'un ostéome ostéoide peut être mise en évidence par l'angiographie. Ce fait peut venir à l'appui du diagnostic radiographique et faciliter le diagnostic différentiel avec l'abcès osseux.

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FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. K. LINDBLOM) AND THE DEPARTMENT OF INTERNAL MEDICINE (DIRECTOR: PROF. H. LAGERLÖF), KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

THE SMALL INTESTINE TRANSIT TIME WITH A PHYSIOLOGIC CONTRAST MEDIUM

by

O. MATTSSON, GUNVOR PERMAN and H. LAGERLÖF

The transit time in follow-through examinations of the gastro-intestinal tract varies considerably, as has been pointed out by many authors. LÖNNERBLAD (1951) and FRENCH (1952) recorded wide variations in normal adults; in children these may be even greater (HENDERSON 1942). It is generally held that the variations found in pathologic cases bear no reliable relationship to the clinical conditions. PYGOTT (1958) claimed that follow-up examinations are of no great value. He stated: 'the radiological examination of the small bowel can be a lengthy procedure and routine requests for a barium meal and follow-through have no justification'.

The ordinary barium meal — generally a suspension of barium sulphate and emulsifying agents in water — will never act as a physiologic stimulator of the gastro-intestinal tract. There is reason to suppose that the absence of nutrients is responsible for this negative effect.

Barium meals containing food are by no means a novelty. References may be made to KOLTA (1931), and to SANDSTRÖM & HALLBERG (1946). RAVDIN et coll. (1936) and others have suggested that fat, protein and carbohydrate

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sh ıld be added to produce more physiologic conditions for the examination of he transit time. FRENCH (1952) pointed out that the administration of fo l with the contrast medium is a reasonable procedure in assessing the rate of assage, but he noted that there seems to be no standardization of method. H also pointed out that many studies of the transit time bear only a superfic l relationship to the main problem which is the rate of passage of food an not of a contrast medium through the small intestine.

ttempts made up to now to use mixtures of barium sulphate and nutrients or ood products do not seem to have proved satisfactory. This may be explained by the fact that flocculation, or the formation of lumps, or sedimentation must have occurred and adversely affected the end-results of the examination. The most important demands on a barium meal are that the contents should be completely homogeneously mixed, that the mixture should remain stable, and that the roentgenographic depiction of the anatomy should be accurate. A special barium sulphate preparation with a very low tendency to sedimentation was tested (EMBRING 1956, MATTSSON 1956). The stability is based on the presence of minimal quantities of alkaline salts of certain organic and inorganic acids. The preparation is a powder, and is particularly pure (98 % $BaSO_4$) and is liable to minimal sedimentation in mixtures.

BORGSTRÖM et coll. (1957) have studied by chemical analysis the intestinal absorption of bowel contents collected by intestinal tubes. By such investigations information is obtained regarding the absorption of different food components, and an analysis of the successive stages of digestion is thus possible. By using the same nutrient components, the physiologic behaviour of which is known by tube analysis, and adding the special barium sulphate preparation mentioned above, a test meal suitable for roentgenologic examination was obtained. The composition of the nutrient part of the test meal is given below:

	g	Fat	Carbohydrate	Protein
Corn oil	74	74	—	—
Skim milk powder	126	0.5	50	63
Dextrose	138	—	138	—
P E G*	5	—	—	—
Serum albumine	1	—	—	1
Water	1 000	74.5	188	64
mg per ml:		60	150	50

The caloric content of the meal: 1.25 cal/ml

* P E G (polyethylenglycol) is used as a non-absorbable reference substance. (Cf. the Diagram on next page.)

The nutrient component which is prepared by the dispensary of the hospital is mixed with the barium, the proportion being the same in all cases — two parts of barium to three parts of the food component measured by volume. In vitro tests with the mixture showed that within some hours there was only

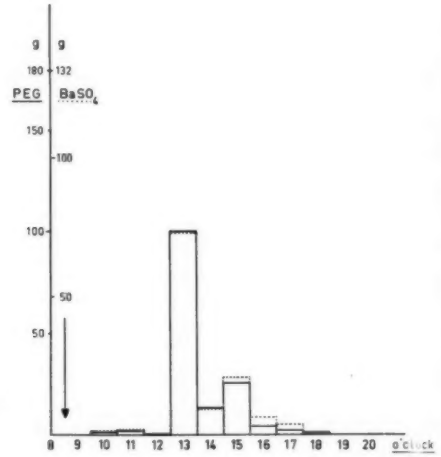

Diagram showing identical passage conditions for the barium sulphate and the polyethylenglycol in a case of ileostomy.

an insignificant separation of a small layer of fat and there was no sedimentation of importance. These experiments were made in test tubes which were not moved. In practice the slight tendency to sedimentation will be counteracted by the intestinal movements. In spite of the mixing with juices from all the digestive glands the meal appears to remain remarkably homogeneous during its passage through the intestinal tract. Fig. 1 shows a roentgenogram of the stomach and the duodenum.

The barium sulphate preparation travels at the same rate as the nutrient component during their passage through the small bowel. This was demonstrated in two cases of ileostomy near the ileocaecal valve. Analysis of the intestinal contents from the ileostomy showed that the barium sulphate and the non-absorbable polyethylenglycol were present in the same proportions as when originally ingested (Diagram above).

Method

The patients came to the roentgen department without having had anything to eat or drink since the previous evening. All examinations started early in the morning and nothing else was taken by mouth until at least four hours later. The patients had their luncheon and evening meal as usual. The barium-food meal is rather like gruel and seems to be palatable to most of the patients. It was served at a temperature of 20° C. The same volume, 300 ml, was given in all cases. The food value is about 375 calories. The patients were up and about and came for examination at fixed times; none was confined to bed. They did not lie on the right side, and the emptying of the stomach was thus not accelerated. Changes in the patient's ordinary conduct of life were avoided.

Fig. 1. The mucosal pattern of the stomach and duodenum with the physiologic contrast meal.

The films were obtained at fixed intervals, the first one 15 min after ingestion of the meal. The subsequent films were taken at 30 min, 1 hour, $1^1/_2$ hours, 2 hours, and thereafter at intervals of one hour until all the contrast medium had left the ileum. In some cases, with very prolonged transit times, longer intervals towards the end of the period of examination were chosen. The time of the actual exposure of the film was kept with the greatest possible accuracy, a special section of the roentgen department being placed at the disposal of these patients who were examined outside the ordinary routine work by special personnel. The psychologic mood of the patient is of great importance when studying the intestinal passage (GOIN 1954). A calm undisturbed atmosphere is as important as the time accuracy of a fixed program, and will render accurate comparisons possible. All patients were examined supine in the p.a. projection with the roentgen tube above the couch so as to ensure standardized conditions.

To reduce the dose to the gonads a sheet of lead rubber was placed on the pelvis in such a way as not to mask the contrast filled intestines. (See Fig. 4 in which the lead protection is visible at the bottom in some of the films.)

The speed of the transportation of the test meal was analysed by recording: when the first portion of the meal had reached the L5—S1 level (1), when the fundus of the caecum was filled (2), when the stomach was completely empty (3) and when all the contrast meal had reached the colon (4).

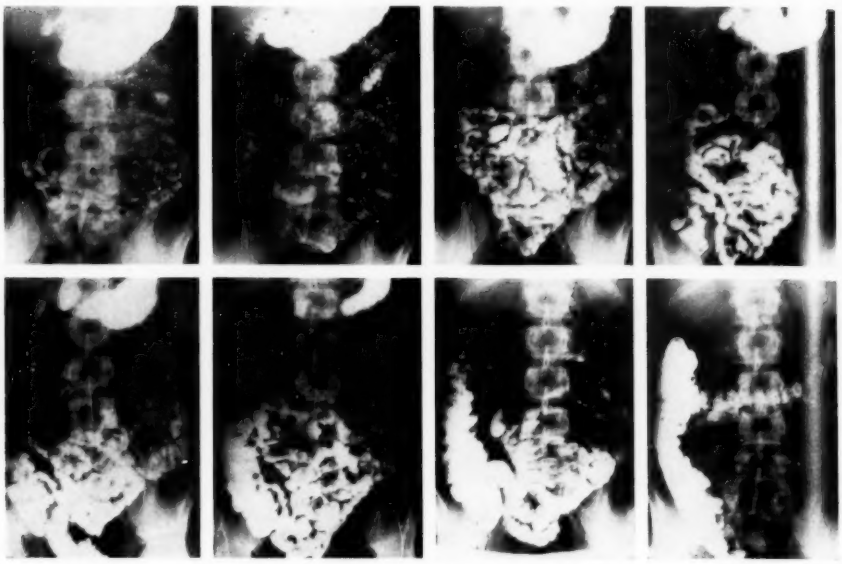

Fig. 2. Healthy student, aged 23. Films taken at 15 min, 30 min, 60 min, 90 min and 2, 3, 4 and 5 hours after the meal. The first small portion of the meal passes rapidly through the small intestine the remainder of the meal gradually filling it.

Material and Results

Normal cases. There are 30 normal cases in our material. The ages of the patients, women as well as men, ranged between 17 and 71 years.

The first portion of the meal ran rapidly through the small bowel, and in the first film had already reached the true pelvis, a small amount of the meal being regularly distributed between this region and the stomach. Later on the small intestine filled up more and more, mainly by an increase in its lumen. After about 2 hours the meal started to enter the colon. The transit time through the small bowel was completed after six hours. The stomach was empty after about four hours. Fig. 2 shows a series of films of a normal case.

Pathologic cases. Well defined pathologic conditions in the gastro-intestinal canal are represented by the following 48 cases:

Total gastrectomy	4
Partial gastrectomy without 'dumping syndrome'	6
Partial gastrectomy with 'dumping syndrome'	12
Pancreatic steatorrhea	10
Nontropical sprue — steatorrhea	7
Ulcerative colitis	9

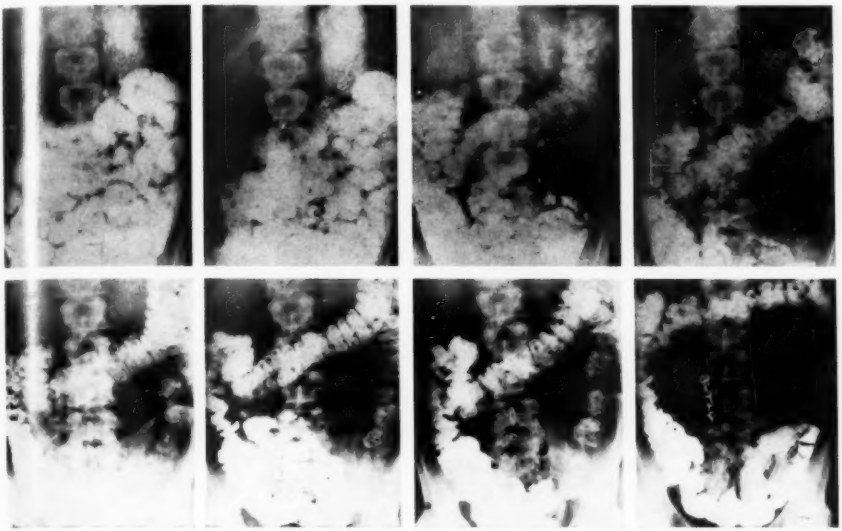

Fig. 3. Male aged 58. Gastrectomy 7 years previously. Severe 'dumping symptoms' after meals. Films taken at 15 min, 30 min, 60 min, 90 min, and 2, 3, 4 and 5 hrs after the meal (Cf. fig. 2). Rapid and extensive filling of the entire small intestine and early filling of the colon.

In order to determine whether the small intestine transit time is dependent on the rate of emptying of the stomach, four patients with total gastrectomies were examined. The L5—S1 level was reached in the film obtained 15 min after the ingestion of the meal, as in normal cases. In one of the four cases of total gastrectomy the fundus of the caecum was reached after two hours, and in the others in shorter times than any of the normal cases. It took longer for the entire contrast meal to leave the small intestine than in the normal group.

Eighteen patients with partial gastrectomies were examined. The gastric remnant was empty after about three hours. In the 12 cases, which had moderate or marked dumping, the caecum was reached in 15 to 30 min, as against the remainder without dumping which behaved as the normal group. The whole meal had left the small intestine in 6 to 8 hours, the somewhat longer times being found in the cases with dumping symptoms. Fig. 3 shows a series of films typical for a case of severe dumping.

Seventeen cases of steatorrhea were examined. Seven of these had a normal secretin test but deficient absorption of B_{12} and a positive xylose test. The clinical diagnosis was nontropical sprue. A typical series of films is shown in Fig. 4 and 5. In 10 cases the steatorrhea was caused by pancreatic achylia

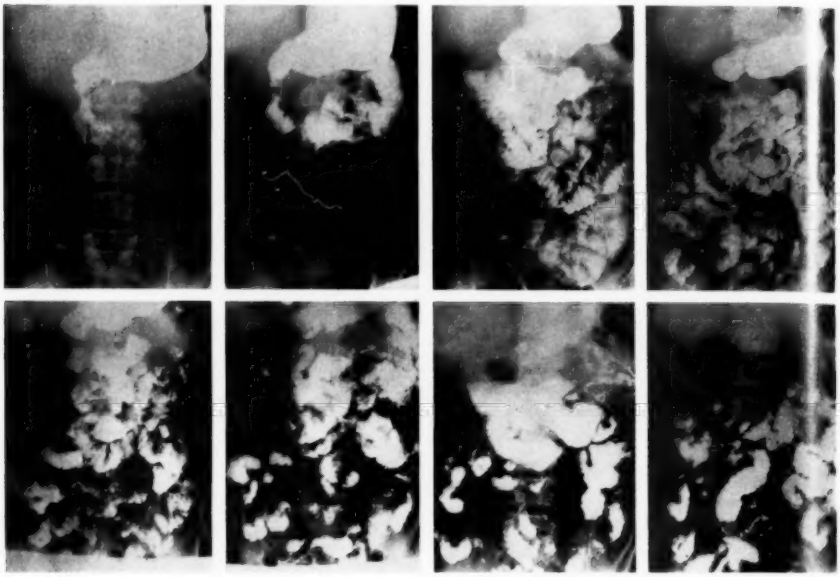

Fig. 4. Male aged 55, with steatorrhea (sprue syndrome). Films taken at same intervals as in figs 2 and 3. The filling of the small intestine is very different from the normal and particularly marked in the first films. The L5—S1 level is reached much later and the caecum is not filled until 7 hours after the meal. The emptying rate of the stomach, on the other hand, is unaltered. Cf. fig. 5, representing later films.

as shown by secretin tests. On an average the contrast meal reached the caecum much slower in the cases of this condition than in the other groups examined. The total transit time was also prolonged.

The small intestine transit time in 8 cases of ulcerative colitis did not differ systematically from the normal group.

The most important data from the normal cases and the pathologic cases are assembled in Table 1. The statistical differences between the pathologic groups and the normal are presented in Table 2.

Discussion

The transit time through the small intestine studied roentgenologically with conventional barium contrast media shows great variations in normal subjects (FRENCH, LÖNNERBLAD, and others). On the other hand, surprisingly uniform results have been obtained in the present investigation. These appear to be due to the administration of a barium contrast preparation of good suspension stability mixed with a food material containing carbohydrate, fat

Table 1

The small intestine transit time (given in hours) in the normal group and in some of the pathologic groups

	Stomach completely empty	Contrast reaches S5—S1 level	Meal appears in caecum	Meal has left term. ileum
Mean value	4.2		1.9	6.3
Range	2.3—8	0.25—0.50	0.5—4	4—8
95 % confidence limit	2.0—7.1		0.5—3.9	4.2—8.7
Partial gastrectomy without 'dumping syndrome'				
Mean value	3.0		1.7	7.1
Range	1.5—4	0.25—1	1—3	5—9
95 % confidence limit	1.0—6.1		0.3—4.1	3.6—12.0
Partial gastrectomy with 'dumping syndrome'				
Mean value	2.8			8.2
Range	1—4	0.25	0.25—0.50	6—10
95 % confidence limit	0.8—6.1			5.4—11.8
Pancreatic achylia				
Mean value	6.9		5.3	11.3
Range	3—12	0.25—0.5	3—9	7—24
95 % confidence limit	1.4—16.8		2.5—9.1	3.4—23.8
Non-tropical sprue syndrome				
Mean value	7.0		4.7	13.1
Range	4—10.5	0.25—1	3—8	9.5—18
95 % confidence limit	2.1—14.8		1.7—9.4	7.3—20.5
Ulcerative colitis				
Mean value	5.2		1.8	9.7
Range	3—12	0.25—1	1—3.3	7—12.5
95 % confidence limit	0.4—15.4		0.3—4.5	6.9—13.1

and protein, and thus a physiologic stimulant of the digestive tract. The details of the method of examination were standardized. Short intervals between the films at the beginning of each test are particularly important since the first part of the meal passes rapidly down the small intestine. It is also necessary to extend the time of observation sufficiently, until the whole of the meal has left the small bowel. There seems to be no correlation between the speed of passage of the first and last portions of the meal. As it is believed that psychologic factors influence the small intestine transit time considerably, a calm and unhurried atmosphere was aimed at during the investigation. It is nevertheless surprising that such small variations occurred under the given conditions.

A comparison between the normal small intestine transit time obtained with the present technique and with other techniques is possible only as regards the time of the appearance of the meal in the caecum. In our material

Table 2

Statistical differences between the pathologic and normal groups. Each pathologic group was treated separately in comparison with the normal group. A square root transformation was used to normalize the ... distribution.

	No. of cases	Stomach completely empty	Meal appears in coecum	Meal has l... term. ileu...
Partial gastrectomy with 'dumping'	12	$t = -3.28$ $p = 0.01-0.001$	$p < 0.001$	$t = 4.65$ $p < 0.00$
Partial gastrectomy without 'dumping'	6	$t = 2.22$ $p = 0.05-0.01$	$t = 0.37$ $p > 0.05$	$t = 1.55$ $p > 0.05$
Pancreatic achylia	10	$t = 3.94$ $p < 0.001$	$t = 8.3$ $p < 0.001$	$t = 6.11$ $p < 0.00$
Sprue syndrome	7	$t = 4.24$ $p < 0.001$	$t = 6.55$ $p < 0.001$	$t = 10.47$ $p < 0.00$
Ulcerative colitis	9	$t = 1.53$ $p > 0.05$	$t = 0.0055$ $p > 0.05$	$t = 7.41$ $p < 0.00$

the fundus of the caecum was normally reached after about two hours, as against experiences with conventional barium meals, where longer times seem to be the rule.

It might be expected that the small intestine transit time would depend upon the emptying time of the stomach. This is not so however. In one case of total gastrectomy, for example, the transit times of the first portions of the meal were normal.

In contrast to earlier reports the gastric remnant in cases of partial gastrectomy does not empty rapidly, whether or not there are any clinical signs of the dumping syndrome. This is particularly noticeable as the meal is fluid. The material needs to be extended, but the present observations show that a small part of the meal passes down the small intestine as the result of an intense peristaltic rush and is found in the caecum after 15 minutes. The difference from the comparatively slow propagation of the first part of the meal in normal cases, and in cases of gastrectomy without the dumping syndrome, is striking.

According to Bossak, Wang & Adlersberg (1957) there appeared to be no constant small intestine transit time in malabsorption with steatorrhea. Using the conventional technique he reported an equal distribution of rapid and prolonged passages. In the present investigation all the steatorrhea cases had slow transit times. This difference seems to be due to the physiologic contrast meal. Some of the cases were examined with a conventional contrast meal as well, and large discrepancies were found. In one case, for instance, the fundus of the caecum was reached after one hour when the ordinary technique was employed but not until nine hours when the physiologic contrast meal was administered.

Eight cases with ulcerative colitis and diarrhoea were examined; the small intestine transit time was found to be normal or slightly delayed. Thus the

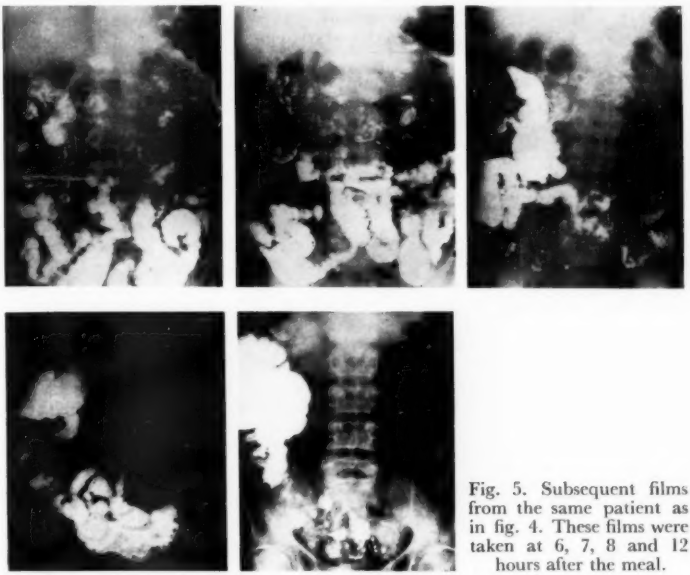

Fig. 5. Subsequent films from the same patient as in fig. 4. These films were taken at 6, 7, 8 and 12 hours after the meal.

diarrhoea appears to be due only to the inability of the colon to absorb water and to store the solid contents; as the colon is successively filled it empties at the same rate, and only relatively small amounts of contrast medium remain in its lumen. These traces of contrast material are, however, often sufficient to permit a rough roentgenologic assessment of the conditions of the colon.

SUMMARY

A method of studying the gastric emptying time and the small intestinal transit time roentgenologically by means of a special meal is described. These times in 48 cases in six different pathologic groups showed characteristic deviation from those recorded in 30 normal cases.

ZUSAMMENFASSUNG

Eine Methode zum Studium der Magen-Entleerungszeit und der Dauer der Dünndarmpassage mittels einer speziell hergestellten Mahlzeit wird beschrieben. Diese Passagezeiten von 48 Fällen, die in 6 verschiedene pathologische Gruppen unterteilt waren, zeigten charakteristische Abweichungen von den Untersuchungsresultaten 30 normaler Fälle.

RÉSUMÉ

Les auteurs décrivent une méthode pour étudier radiologiquement, au moyen d'un repas baryté spécial, la durée de l'évacuation gastrique et du transit dans l'intestin grêle. Dans 48 cas répartis en six groupes pathologiques différents, ces durées ont présenté une différence caractéristique par rapport aux durées observées dans 30 cas normaux.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROF. ERIK LINDGREN), SERAFIMER-LASARETTET, STOCKHOLM, SWEDEN

WIDTH OF THE COMMON BILE DUCT BEFORE AND AFTER MORPHINE STUDIED BY CHOLEGRAPHY

by

MATS JONSON

Many opinions have been expressed regarding the diagnostic significance of the width of the large bile ducts. However, what is known with certainty today is that these ducts show considerable variations in width in both normal and pathologic materials, that they are often but not always wider in cholecystectomized than in non-operated cases, and that they in many instances dilate under the influence of morphine. As no satisfactory explanation of these observations has yet been advanced, the present investigation was undertaken in an endeavour to obtain useful information from a series of intravenous cholegraphies showing definite contrast filling of the bile passages.

Material. The material consists of 100 cholegraphies carried out in 100 non-operated cases, and 100 similar examinations in an equally large group of cholecystectomized cases. Only those cases in which the bile ducts were demonstrated distinctly enough to allow measurement of their width were chosen for study. Nor were any cases included in which the administration of morphine was not possible because of previously known hypersensitivity. No other selection of the material was applied, the cholegraphies studied being those performed in routine succession at the hospital.

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From the diagnostic standpoint, the 100 cholegraphies performed in th non-operated cases were distributed as follows:

Normal findings		39 case
Pathologic findings		61 case
Calculi in the gallbladder but not in the bile ducts	29 cases	
Calculi in both the gallbladder and the ductus choledochus	7 cases	
Calculi in the ductus choledochus but not in the gallbladder	1 case	
Gallbladder not demonstrated; no calculi in the bile ducts	20 cases	
Gallbladder not demonstrated; calculi in the ductus choledochus	4 cases	

Among the 100 cholegraphies carried out in the cases subjected to cholecystectomy there were 5 with calculi in the common bile duct.

Technique. Following an intravenous injection of 20 ml Biligrafin-forte roentgenograms were taken at intervals of 15, 30 and 45 minutes with the patient in the prone position. Fifty minutes after injection of the contrast medium morphine (0.1 cg per 10 kg bodyweight) was given subcutaneously and roentgen films were taken 10 and 20 minutes afterwards. As a final measure the patient received a spasmolytic (Recipavrin, 1 ml intravenously) and films were obtained 5 and 10 minutes after this injection. In a few cases, 4 drops of nitroglycerin sublingually were given instead of Recipavrin and films obtained at 1 min intervals. Tomography was carried out in the majority of cases while the bile ducts were under the influence of morphine.

Results

The width of the common bile duct was measured both before and after the morphine injection, the common hepatic and common bile ducts being counted as one unit. In films obtained before the injection, a measurement was made at the widest part of the duct, and the same site was measured again on films taken about 20 min after the administration of morphine. The figures obtained from the films have not been corrected for magnification, which amounts to 10 to 20 %. The varying magnification, which was due to different object-film distances (6 to 12 cm), did not affect the figures to such a degree that correction was considered necessary. The width of the common bile duct before the morphine injection in the non-operated and in the cholecystectomized cases will be seen in Table 1.

In the non-operated group, there was a marked difference between cases with normal roentgen findings and those with pathologic features, the bile

Table 1

	Non-operated cases		*Cholecystectomized cases*	
	No. of cases	*Width of common bile duct*	*No. of cases*	*Width of common bile duct*
tal material	100	7.6 mm (3—17 mm)	100	9.1 mm (3—22 mm)
ses with normal roentgen findings	39	5.9 mm (3—11 mm)	—	—
ses with pathologic roentgen findings	61	8.7 mm (4—17 mm)		

ucts being wider, on an average, in the latter cases. The difference is statistically significant.

The ducts in the cholecystectomized group were in general slightly wider than in the non-operated cases, but it will also be noted that the common bile duct in the surgically treated cases was approximately of the same width as the ducts in the non-surgical cases with roentgenologically demonstrable biliary disease. The latter category is precisely the group from which cholecystectomy cases are collected. It would therefore seem as if the cause of the dilatation of the common bile duct lay not in the operation but in the disease that had occasioned it. Whereas all the wide ducts were found among the surgically treated cases or in those with roentgenologically demonstrated biliary disease, normally wide or even very narrow ducts were present in all groups.

It has long been considered an axiom that dilatation of the bile ducts arises after cholecystectomy. Observations made in animal studies by ODDI, VAN HENGEL, HAUTEFORT, JUDD and MANN, and others, have been cited in support of this view, while critical opinions such as those of NASSE have received little attention. Of late, however, more emphatic doubts have been raised, by SAMUEL among others, regarding the postoperative dilatation in man. LE QUESNE et coll., who recently compared the width of the common bile duct in operative cholangiographies, and in cholegraphies performed in the same patients some time after the operation, found that the ducts were not dilated after the intervention. The writer's material confirms these observations in all respects.

Various morbid conditions in or around the biliary ducts may cause them to dilate. Stenosing processes, for instance, always have this effect, and among other conceivable causes the passage of gallstones has been mentioned by COURVOISIER as likely to produce dilatation in the majority of cases. Other investigators, however, consider that suspended gallbladder function, whether it be due to infection, gallstones, or cholecystectomy, is the main factor underlying dilatation of the ducts. NUBOER held that Oddi's sphincter hypertrophies when the gallbladder is out of function, and that this could cause secondary widening of the biliary ducts. According to other authors, hypertrophy and infection of Oddi's sphincter may lead to constricting papillitis, with dilatation as the result (DEL VALLE and DONOVAN; MALLET-GUY et coll.). ROST emphasized the

Table 2

	No. of cases	*Average width of common bile duct*
Contrast-filled gallbladder without calculi	39	5.9 mm
Contrast-filled gallbladder containing calculi	37	8.7 mm
No filling of gallbladder	24	9.0 mm

Table 3

Non-operated cases	12	12.1 mm (6—17 mm)
Surgically treated cases	5	12.8 mm (7—16 mm)

Table 4

Small calculi, typical biliary colic	18	9.9 mm (5—15 mm)
Large calculi, diffuse epigastric pain	14	5.9 mm (4—9 mm)

significance of the anatomy of the sphincter in the occurrence of dilatation of the common bile duct, suggesting that the longer the sphincter, the more effective is the contraction and the more favourable are the conditions for biliary duct widening. BERGH, SANDBLOM and IVY thought that sphincteral insufficiency might produce dilatation of the common bile duct as a result of transmission of the duodenal pressure upwards into the duct.

In order to gain some idea of how the gallbladder function affects the width of the common bile duct the present non-surgical material was divided into 3 groups, i. e. cases with a contrast-filled gallbladder without calculi, cases with a contrast-filled gallbladder containing calculi, and cases with no filling of the gallbladder (Table 2).

It appears from Table 2 that in many of the cases with a pathologically changed gallbladder there was also dilatation of the ducts. Defective gallbladder function does not seem to have caused any appreciably greater widening than the presence of calculi in a gallbladder with retained function.

Table 3, showing all the cases with stones in the bile ducts, was compiled to investigate the possible relation between biliary duct calculi and dilatation of the common bile duct. The width of the duct in these cases may be studied in the table.

To throw further light on the significance of gallstones, a comparison was made between two groups of cases with biliary concretions. One group contained cases with small stones not exceeding 5 mm in diameter and typical attacks of biliary colic in the clinical history; in the other group, the stones were greater than 5 mm in diameter and the patients had suffered from diffuse pain in the epigastric region without typical biliary colic. The width of the common bile duct in these two groups is shown in Table 4. The figures in this table support unequivocally the view, previously advanced by COURVOISIER, that dilatation of the common bile duct is usually related to the passage of gallstones.

All cases in the present material were given morphine with a view to producing contraction of Oddi's sphincter. It is difficult to obtain an objective

easure of the diagnostic value of morphine in cholegraphic studies. Many thors assert definitely that morphine medication improves the examination chnique. Discomfort in the form of biliary pain, nausea, and vomiting are, wever, side-effects to which attention should be paid (DEBRAY, JOURDE et CANUET, and others). HORNYKIEWYTSCH, who has studied functional changes sociated with the passage of bile through Oddi's sphincter, maintained that a agnosis regarding function is not possible after administration of morphine. RIANOFF, HENRARD et VAN ROSSUM, on the other hand, considered that morphine medication forms part of the examination in an investigation of the function of Oddi's sphincter. GUNNARSON, who studied dilatation of the common bile duct after the administration of morphine in a series of cholecystectomized cases, correlated his observations with the occurrence and severity of dyskinesia symptoms. His results suggested that the dilatation of the duct following morphine medication is greater in proportion to the severity of the dyskinetic symptoms. As opposed to this statement, we have BORIS and LÖRINC's assertion that the value of morphine lies in the increased contrast density obtained in the ducts but that it is of no significance in the diagnosis of dyskinesia.

An attempt was made to evaluate the significance of morphine in the 100 cholecystectomized cases in the present material. It was found that in 49 % of the cases the contrast density in the bile ducts was much better after the administration of morphine than before. In 12 % of the cases, this increase in contrast density was a decisive factor in the definite establishment or exclusion of pathologic changes. Another way in which morphine improves the examination technique is that the bile passages remain filled with contrast medium for a relatively long period; this is often of value when tomography is to be carried out. It would thus seem advisable to administer morphine in all cases in which the demonstration of the bile ducts is not satisfactory enough for diagnosis 45 to 60 minutes after injection of the contrast medium. The commonest discomfort, biliary pain, can usually be rapidly relieved by the administration of a papaverine derivative or of nitrites.

GUNNARSON's results suggested that there is a correlation between dyskinesia and dilatation of the common bile duct following morphine medication. His material was divided into four groups according to the degree of the dyskinetic symptoms, which were apparently classified more on the basis of frequency than of intensity and duration. Although it is always difficult to make comparisons between different materials, an attempt has nevertheless been made to compare the present series with GUNNARSON's cases. All cases in which the clinician could not make a definite diagnosis between dyskinesia or some other condition were rejected. Choledocholithiasis cases were also excluded. After this reduction of the material, 44 surgically treated cases remained; these were distributed as shown in Table 5 and in the Diagram on next page.

For the whole of this material, the mean for the dilatation following morphine medication was 23 %, a figure corresponding almost exactly to that mentioned

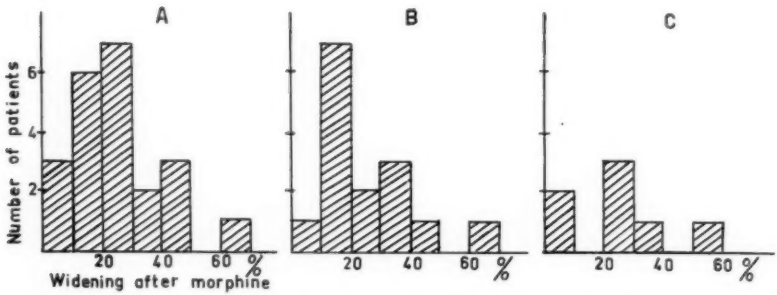

Diagram representing the dilatation of the common bile duct in 44 cases distributed according to the degree of dyskinesia symptoms. A — no dyskinesia, B — mild to moderate, and C — severe dyskinesia.

by GUNNARSON (24 %). In other respects, however, the results did not confirm GUNNARSON's observations. Thus, this material gives no indication that there is any connection between the severity of dyskinesia symptoms and the degree of dilatation of the common bile duct after administration of morphine.

One of the difficulties involved in the interpretation of dyskinesia cases lies in the indefinite nature of the dyskinesia syndrome. The majority of the cholegraphics carried out in the surgically treated cases were undertaken because of symptoms suggesting genuine biliary dyskinesia, but in many cases the symptoms were too undefinable to allow an exact diagnosis to be made. Many investigators hold that it is common for patients with typical biliary dyskinesia to react to morphine with pain. SKLAROFF et coll. considered that in addition to dilatation of the lumen and increased contrast density in the bile ducts, pain is experienced in the region of the ducts in dyskinesia cases. LAGERLÖF even based the diagnosis of biliary dyskinesia on the occurrence of pain in the biliary region following morphine medication, at least in those cases in which roentgen examination of the alimentary tract and kidneys was negative.

The relation between clinical dyskinesia symptoms and morphine-provoked pain in our material is shown in Table 6.

This material thus gives added support to the view that dyskinesia cases react to morphine with pain to a greater extent than other cases. None of the choledocholithiasis cases reacted to morphine in this way. When the dilatation of the common bile duct before and after morphine medication was judged on the basis of the pain reaction, the results shown in Table 7 were obtained.

Table 5

	No dyskinesia symptoms	*Mild to moderate dyskinesia*	*Severe dyskinesia*
Number of cases	22	15	7
Dilatation following morphine .	24 % (0—67 %)	23 % (0—60 %)	21 % (0—55 %)

Table 6

	No dyskinesia symptoms	*Dyskinesia symptoms*	*Choledocho-lithiasis*	*Uncertain pain*
Number of cases	22	22	5	51
No pain after morphine	13	2	5	30
Pain in biliary region after morphine	9	20	—	21

Table 7

	No. of cases	*Width of common bile duct before morphine*	*Dilatation after morphine*
Total material	100	9.1 mm (3—22 mm)	22 % (0—100 %)
No pain after morphine	50	9.8 mm (3—22 mm)	22 % (0—100 %)
Pain after morphine	50	8.5 mm (4—19 mm)	23 % (0— 60 %)

As a comparison, the corresponding figures for the entire non-surgical material are given below:

Number of cases	*Width of common bile duct before morphine*	*Dilatation after morphine*
100	7.6 mm (3—17 mm)	19 % (0—75 %)

Of these non-operated cases, 13 had pain resembling biliary colic after the administration of morphine.

Accordingly, to the extent that a pain reaction to morphine provocation can be considered characteristic of biliary dyskinesia, these figures also argue against the possibility of a connection between dyskinesia symptoms and bile duct dilatation following the administration of morphine. In our opinion, dilatation of the bile ducts after morphine possesses little diagnostic significance. On the other hand, our material appears to confirm the view expressed by LAGERLÖF, as well as by SKLARAFF et coll., and other investigators, that pain in response to morphine medication is a symptom occurring more often in dyskinesia cases than in other patients.

SUMMARY

The width of the common bile duct before and after the administration of morphine has been studied in cholegraphies from 100 cholecystectomized cases and 100 non-surgical cases. The effect of calculi and cholecystectomy on the duct width is discussed and the advantages of morphine medication in cholegraphy stressed. Doubt is expressed regarding the diagnostic value of widening of the common bile duct following morphine medication.

ZUSAMMENFASSUNG

Die Weite des Ductus choledochus wurde mittels Cholegraphie bei 100 cholezystektomierten und 100 nicht-chirurgischen Fällen vor und nach Verabreichung von Morphin studiert. Es wird die Wirkung von Konkrementen und Cholezystektomie in Bezug auf die Weite des

Ductus besprochen und die Vorteile der Morphinmedikation bei der Cholegraphie hervorgehoben. Es werden jedoch Zweifel bezüglich des diagnostischen Wertes einer Erweiterung des Ductus choledochus nach Morphininjektion erhoben.

RÉSUMÉ

L'auteur a étudié, sur les cholegraphies de 100 malades cholécystectomisés et de 100 malades non chirurgicaux, la largeur de la voie biliaire principale avant et après administration de morphine. Il examine l'effet des calculs et de la cholécystectomie sur la largeur de la voie biliaire et souligne les avantages de l'épreuve à la morphine au cours de la cholégraphie. Il exprime ses doutes sur la valeur diagnostique de l'élargissement de la voie biliaire principale après l'administration de morphine.

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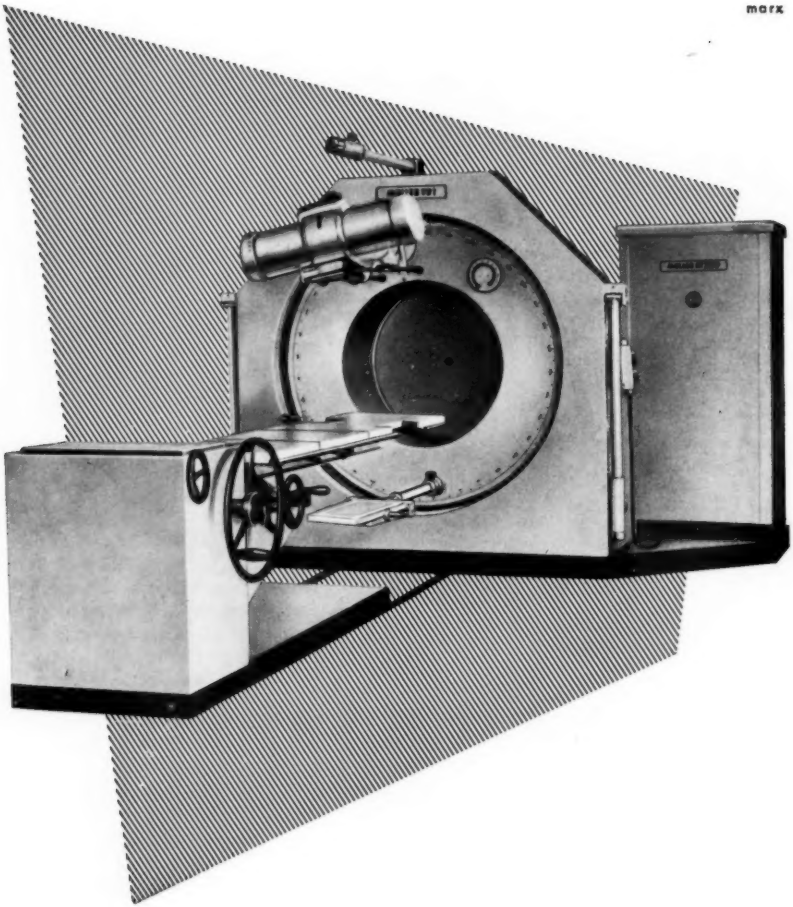

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THE INFLUENCE OF DIFFERENT CONTRAST MEDIA FOR CHOLEGRAPHY ON BLOOD PRESSURE AND PULSE RATE

by

GEORG-FREDRIK SALTZMAN and KARL-ANDERS SUNDSTRÖM

Side-effects from the contrast medium are not uncommon in cholegraphy. SALTZMAN has described the different symptoms and signs that may arise from intravenously administered Biligrafin, and at the same time has reviewed the more important observations in this field published before 1959. FROMMHOLD & BRABAND, and MAURER, have investigated 23 deaths following intravenous cholegraphy. Preliminary experiences with peroral cholegraphy have recently been published by GUNNARSON, SALTZMAN, and VIRTAMA.

Apart from death in connection with intravenous cholegraphy, the most dramatic side-reaction reported is circulatory collapse, which, although uncommon in comparison with the large number of cholegraphies carried out, has nevertheless been described by several authors. Our interest in the effect of the contrast medium used in cholegraphy on the circulation has been further aroused by a case in which symptoms and signs not previously described in such a connection were observed at an intravenous cholegraphy.

Case report

A woman aged 72 had received treatment for several years for cardiosclerosis with auricular fibrillation and hypertension. She also had extensive arterial calcification. A blood pressure of 230/100 had been recorded for several years and this value was also obtained the day before the examination. Immediately after the injection of 20 ml Biligrafin the patient became

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confused and rapidly lost consciousness. About one minute later she was found to have left hemiplegia, and about 10 minutes after the injection a systolic blood pressure of 120 was recorded. Consciousness returned about half an hour after the administration of the contrast medium, and the hemiplegia disappeared rapidly and completely. A neurologist consulted considered transient carotid insufficiency to be the most likely explanation of the patient's reaction.

As far as we can find from the literature no systematic blood pressure determinations have been carried out in connection with cholegraphy, although a few authors have reported a fall in blood pressure after intravenous cholegraphy. HAGEDORN, for instance, noted a considerable decrease in the pressure in a case with circulatory collapse, and PÜSCHEL, who also noted a fall in blood pressure after intravenous cholegraphy, drew attention to the fact that the systolic pressure showed a greater decrease than the diastolic.

The 23 deaths after intravenous cholegraphy described by FROMMHOLD and BRABAND and by MAURER possess certain features in common. Most of the deaths in which a direct connection was considered to have existed between the contrast injection and the fatal outcome occurred in elderly patients. Cardiovascular disease had previously been established in many of the cases; a pressure fall was noted in the one case in which the blood pressure was recorded.

A decrease in the blood pressure has been demonstrated with other water-soluble iodine compounds that have been administered intravenously (ROBB and STEINBERG, and others) or intra-arterially (LINDGREN and TÖRNELL).

The object of the present investigation was to study in an unselected series of cases the effect on the blood pressure and pulse rate of different contrast media used for cholegraphy.

Material and Methods

Intra-arterial blood pressure measurements were carried out at 16 intravenous cholegraphies, with no pre-medication. The usual test dose of Biligrafin-forte was given 24 hours at the latest before the examination, and all cases showed a negative reaction to this dose. The patients were in a recumbent position throughout the examination. The pressure was recorded through a polythene catheter inserted percutaneously into the brachial artery by the technique described by SELDINGER and by BERNEUS, CARLSTEN, HOLMGREN and SELDINGER. A Swema-Elema mechano-electric strain-gauge transducer and a four-channel direct-writing recorder (Mingograph 42, Elema, Sweden) were used for the measuring and recording work. The pressure was recorded continuously, and the determinations were begun about one minute before the injection of the contrast medium and continued for at least 20 minutes. An electrocardiogram was recorded with one lead the whole time the blood pressure measurements were in progress, and the pulse rate was calculated from the electrocardiogram.

A dose of 20 ml Biligrafin-forte was used as the contrast medium for these examinations, except in one case in which a dose of 40 ml was used. The medium was injected intravenously at varying speeds; in 7 cases it was injected rapidly, i.e. within 14 to 40 seconds, and in 9 at a slower rate, with injection times of 4 to 5.5 minutes. One case occupies an intermediate position, with an injection time of 1 minute 45 seconds. In the case in which 40 ml were administered, the first half of this amount was injected within 4 minutes and the other half within 13 seconds, 15 minutes after the first injection.

Similar intra-arterial pressure measurements were made at 3 peroral cholegraphies, the contrast medium used for these examinations being 6 g Solu-Biloptin (Schering); data on this medium are being published in another connection (SALTZMAN). In addition to the intra-arterial pressure measurements in these 3 cases, blood pressure determinations were carried out in the conventional manner in 8 peroral cholegraphies. In 5 of these cases the contrast medium consisted of 6 g Solu-Biloptin while in the other 3 cases 5 g Bilijodon-Natrium (Leo) in gelatine capsules were administered. The systolic blood pressure was recorded before administration of the contrast medium, and once a minute afterwards, over a period of 15 to 30 minutes.

All the cases had a serum bilirubin concentration of 1.7 mg % or lower. No contrast medium was visible in the bile ducts in 2 cases. In both of these cases the medium used was Biligrafin-forte, given intravenously; one of them had a clinical diagnosis of cirrhosis of the liver (serum bilirubin 1.4 mg %) and the other had bile leakage from the common bile duct through a fistula out to the skin. In all the other cases the contrast density in the bile ducts was diagnostically adequate.

Among the 16 patients who received the contrast medium intravenously, one experienced severe nausea and vomited, and 5 others also had nausea. The remaining 10 patients suffered no discomfort from the medium. Of the 8 patients given Solu-Biloptin orally, 2 had slight nausea and 6 had no reactions. One of the 3 patients who received Bilijodon-Natrium felt sick and vomited, while the 2 others had no reactions.

The average age of the patients was 55.8 years in the intravenous cholegraphy group and 55.6 years in the oral cholegraphy group.

Results

Blood pressure

In addition to the systolic and diastolic blood pressures, mean pressures were also recorded. In a few cases, but not in all, the latter pressures were recorded at a point of time corresponding to the maximum of the pressure variations. The apparatus used did not permit the recording of mean pressures simultaneously with systolic and diastolic pressures. As comparisons made in these cases showed that in the assessment of pressure variations it is immaterial

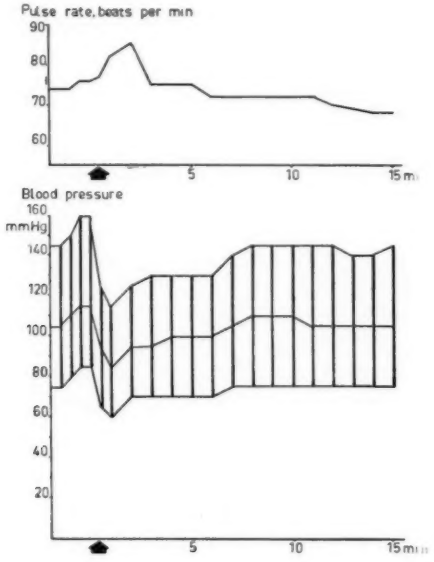

Fig. 1. Blood pressure and pulse rate at intravenous cholegraphy. Rapid injection of 20 ml Biligrafin-forte. Definite blood pressure fall and moderate tachycardia following the injection.

whether mean pressures or systolic pressures are used, the information given in this paper regarding pressure variations refers consistently to the systolic pressures, which were recorded in all cases.

Intravenous cholegraphy. Three of the cases in which intravenous cholegraphy was performed had an increased blood pressure initially, while the other 13 cases had pressures which could be said to lie within the range of normal variations.

A pressure decrease varying from 4 to 38 % was established in all 16 cases in which intravenous cholegraphy was carried out.

In 4 cases, the size of the pressure decrease was more difficult to assess than in the others. These patients had a slight increase in blood pressure immediately before the contrast medium injection, possibly explainable on a psychic basis, and it is difficult to decide which pressure fall was due to the contrast medium, in other words whether it was the smaller decrease, counted from the more constant initial pressure, or the larger decrease, counted from the higher level at which the blood pressure lay at the beginning of the contrast injection. Unless otherwise stated, the smaller pressure decrease is used.

The average pressure fall in these 16 intravenous cholegraphies was 15.5 %. If the larger pressure difference had been chosen in the 4 cases in which the pressure decrease was difficult to assess, the mean fall in pressure amounted

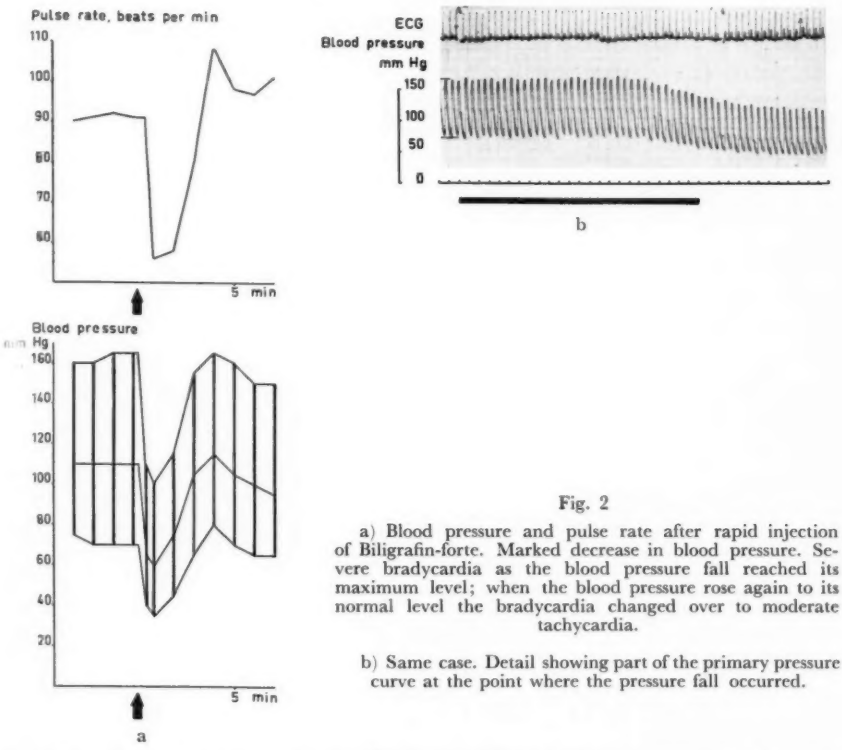

Fig. 2

a) Blood pressure and pulse rate after rapid injection of Biligrafin-forte. Marked decrease in blood pressure. Severe bradycardia as the blood pressure fall reached its maximum level; when the blood pressure rose again to its normal level the bradycardia changed over to moderate tachycardia.

b) Same case. Detail showing part of the primary pressure curve at the point where the pressure fall occurred.

to 17 %. In general, the decrease in pressure was, as a percentage, the same for cases with a high initial pressure as for those in which it was low. It follows from this that when measured in absolute figures the pressure decrease was greater in those cases that had a higher initial pressure.

It is not possible to work out any relation between pressure fall and clinical side-reactions on the basis of this small material. Nor is it possible to establish any definite differences with regard to the relation between the age of the patients and the size of the pressure decrease. It may, however, be mentioned that the greatest fall in the blood pressure was observed in the oldest patient. Among the others as well, there was a tendency for the older patients to show a slightly larger fall than the younger ones. This is remarkable considering the observations made in larger materials (SALTZMAN, THEANDER), which suggested that older patients have fewer clinical side-reactions to Biligrafin than younger patients.

All the pressure measurements referred to in the above figures apply to the 20-minute period during which the continuous intra-arterial measure-

ments were in progress. In one of the cases, a complication arose three hour after the injection of the contrast medium, in other words shortly after th conclusion of the examination. This patient, who was the only one of the 1(patients who had clinically manifest heart disease with auricular fibrillation suddenly showed a fall in blood pressure and became pale and confused The systolic blood pressure was found to be 90 when measured with a pressur cuff. The symptoms disappeared completely within a few hours. The relatio between this complication and the contrast medium injection is naturall uncertain, especially as this patient, like all the others, was given both morphin and nitroglycerine in connection with the cholegraphy. Nitroglycerine cause as we know, a reduction in blood pressure, and dangerous complication following such pressure falls are recognized. A remarkable feature is that thi patient, like the previously mentioned patient in whom transient hemiplegi arose after intravenous cholegraphy, had auricular fibrillation. In the othe cases, no complications were noted after the conclusion of the examination.

As the rate of injection is considered to play a considerable part in producin side-reactions after intravenous cholegraphy with Biligrafin, we carried ou pressure measurements after both rapid and slow injections. In the 7 case in which the contrast medium was injected rapidly, with a mean injectio time of 24 seconds, the average blood pressure fall was 23 % (Figs 1 and 2). In 9 cases in which the injection time varied from 4 to 5.5 minutes the mea pressure fall was 10 % (Fig. 4). One case with an injection time of 1 minut 45 seconds occupies an intermediate position, the pressure fall being 21 % at this examination (Fig. 3).

The decrease in pressure appeared after different lengths of time in th cases with a short injection time and in those given a slow injection. In th former group the fall occurred very early, on an average 40 seconds afte the beginning of the injection (Figs 1 and 2), and in every instance the injec- tion was completed by the time the pressure fall had reached its maximum. With the slow injection the decrease occurred much later, and the slowe the injection the later occurred the pressure fall; in most of the cases it had reached the maximum shortly before the conclusion of the injection (Fig. 4).

The case given a double dose of Biligrafin-forte in slow and rapid injections deserves special mention. After the slow injection, a pressure decrease fro 130/65 to 110/60 was observed after 4 minutes. After 6 minutes the pressur had risen to 120/70 and after 10 minutes had dropped to its lowest valu 95/60. After 12 minutes it had returned to the initial value and stayed at tha level until the rapid injection was started. This was the only case in thi material in which a diphasic reduction in pressure was observed. It is unlikel that the course of this pressure fall, which diverged from that of the othe cases, had any connection with the contrast medium. At the second rapi injection the pressure decreased continuously to its lowest level in the sam way as in the other cases.

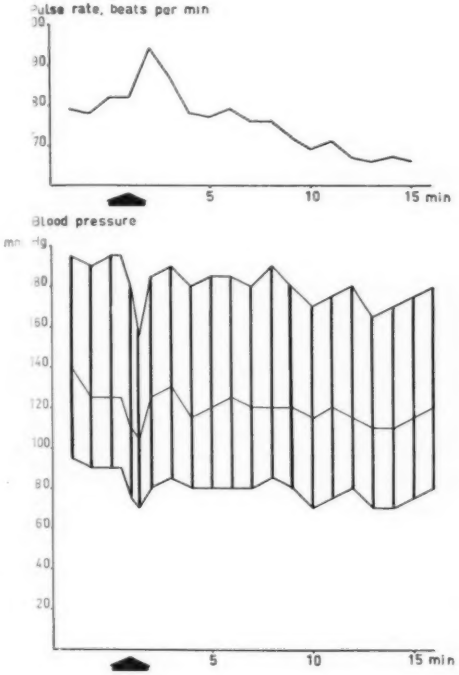

Fig. 3. Moderate blood pressure fall and moderate tachycardia after injection of 20 ml Biligrafin-forte at a speed of 1 minute 45 seconds.

The duration of the pressure fall varied from case to case, the periods of reduced pressure lasting for 2 to 8 minutes in this material. The pressure was decreased over a longer period in the cases with a slow injection than in those in which the medium had been injected rapidly.

As mentioned before, all the blood pressure figures given above refer to the systolic pressure. The diastolic pressure as well fell in all cases. Counted in absolute figures, the decrease in the diastolic pressure was in all cases less than the systolic pressure fall but, as a percentage, the diastolic pressure fall was slightly greater. The mean for the decrease in diastolic pressure was 25 %.

Peroral cholegraphy. All the cases in this material which received Solu-Biloptin perorally as the contrast medium had a normal blood pressure initially. In the 3 cases in which the pressure measurements were carried out intra-arterially a small pressure increase of short duration (3 to 14 %) (Fig. 5) was noted in every instance; in one of them, the pressure rose immediately before the patient began to take the contrast medium. This small increase

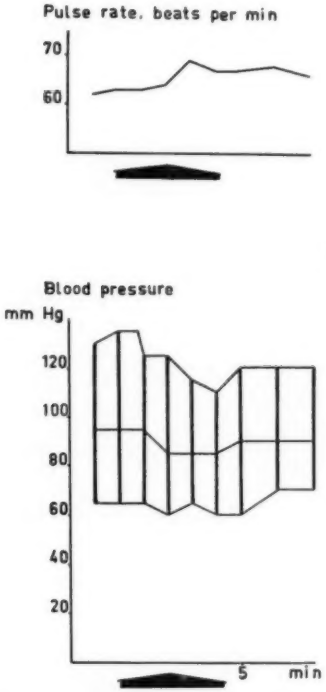

Fig. 4. Slow injection (4.5 minutes) of 20 ml Biligrafin-forte. Slight blood pressure fall and tachycardia.

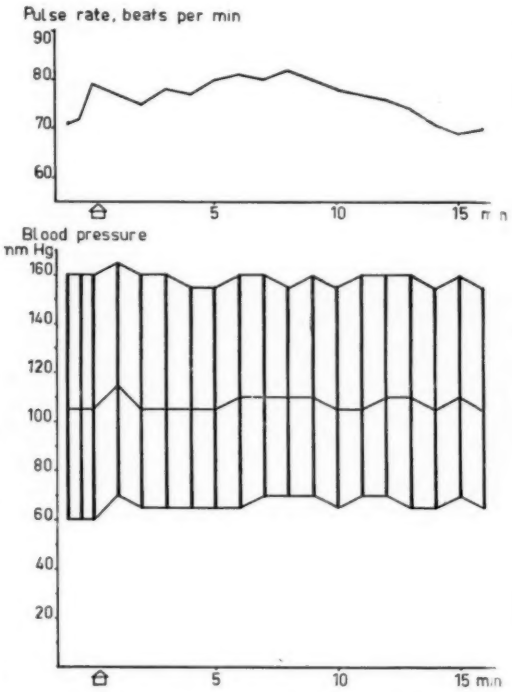

Fig. 5. Blood pressure and pulse rate at peroral cholegraphy with 6 g Solu-Biloptin. No definite effect on the blood pressure. Slight tachycardia.

may probably be explained by the slight physical effort needed to swallow the medium, i. e. to sit up and drink one or two tumblers of water in which it was suspended. A similar result was obtained in the 5 cases in which the pressure measurements were carried out in the conventional manner; a small increase in pressure (7 to 15 %) was noted in 4 cases while in the fifth a very slight decrease (5 %) was recorded. The mean for the pressure changes in connection with peroral cholegraphy showed an increase of 9 %.

The increase in pressure always occurred directly after the contrast medium had been swallowed, and the pressure returned to the initial level within 7 minutes at the latest, in most of the cases within a much shorter time. No complications were reported after the patients had left the roentgen department after the completion of the examination.

In the 3 cases in which Bilijodon-Natrium was used for the cholegraphy no changes in the blood pressure exceeding 5 % were noted.

Pulse rate

Intravenous cholegraphy. The pulse rate showed a moderate increase in the majority of the cases examined by intravenous cholegraphy. No change in the rate was recorded in 3 cases, and in 11 of the other 13 cases it increased by from 5 to 28 %. In the remaining 2 cases fairly large changes were noted. In one of these cases the pulse rate decreased first by about 40 % at the same time as the greatest blood pressure fall in the material was established (Fig. 2). When the blood pressure rose again, the pulse rate also increased and quickly reached a level 20 % above the initial rate. In the other case the pulse rate increased by more than 120 %. As some difficulty was experienced in this case in introducing the catheter for the pressure measurements this probably had a psychic effect on the patient. Both these cases had reactions in the form of severe nausea following the injection of the contrast medium.

The increase in the pulse rate was greater in those cases in which the medium was injected rapidly (Figs 1 and 3). The mean increase was 30 % for these cases, but it should be remembered that the case with a pulse increase of 120 % contributed in large part to producing this high figure. The mean for the other cases was 15 %. For the cases in which the injection was performed slowly the mean increase was 7 % (Fig. 4). All cases without an increased pulse rate are included in this group.

Peroral cholegraphy. An inconsiderable increase in the beat frequency was observed in 2 of the 3 cases examined by peroral cholegraphy in which the pulse rate was recorded in connection with the intra-arterial pressure measurements (Fig. 5).

Discussion

It is evident that the use of Biligrafin as a contrast medium causes a blood pressure fall that may be considerable, and it would seem reasonable to suspect that many of the serious complications that have occurred in connection with Biligrafin injections, while few in themselves, have been directly connected with this decrease in blood pressure. In all the cases in FROMMHOLD and BRABAND's material in which the description of the symptoms from the moment of the injection of the contrast medium to the death of the patient permit an interpretation of the case to be attempted, it must be considered highly probable that the clinical picture developed as a result of a decrease in blood pressure. At least the majority of the patients probably died of heart-failure after a fall in blood pressure had caused cardiac muscle hypoxia with accompanying ventricular fibrillation. In the 2 cases with a clinical picture of pulmonary oedema, which was interpreted by these investigators as a genuine allergic reaction, the condition may well have developed as a result of a failing left ventricle. In all probability the blood pressure fall has little

clinical significance in young patients with a normal heart, but there seem little doubt that it involves a considerable risk in older patients in genera and in patients with cardiovascular disease in particular. It is natural tha patients with blood vessels affected by arteriosclerosis, or with a cardiac function no longer possessing the same capacity for adaptation as in earlie years, should have difficulty in meeting the demands placed on the power of adjustment by a sudden fall in blood pressure. The patient with transien hemiplegia described earlier in this paper was 72 years old, and most of the deaths assembled by FROMMHOLD and BRABAND referred to elderly subjects. The increase in pulse rate observed in the majority of cases after a Biligrafin injection may probably be regarded as a compensatory reaction connected with a fall in blood pressure.

One of the present writers (SALTZMAN) maintained in an earlier publication that a slow injection is probably not more likely to reduce the side-effects than a rapid one. However, the observations in the present investigation demonstrate that a slow rate of injection results in a smaller blood pressure fall than a rapid rate. The apparently incorrect view that the injection rate is of no significance probably arose because, at a comparative investigation, a rapid contrast injection was carried out in the same patient only 45 minutes after a slow one. LINDGREN and SALTZMAN demonstrated later that a cat given several Biligrafin injections one after the other reacts with a smaller blood pressure fall in the later injections than in the first. This observation is probably applicable in man as well.

No decrease in blood pressure occurred in peroral cholegraphy with Solu-Biloptin. The side-reactions hitherto observed with this preparation have been slight. Although there is no justification as yet for entirely excluding the possibility of serious reactions with this medium, seeing that it has only been used on an experimental scale, it looks as if the risk of complications due to a blood pressure fall could be greatly reduced, perhaps even eliminated, if cholegraphy were carried out with the aid of orally administered Solu-Biloptin. The same assumption probably applies to Bilijodon-Natrium.

These observations indicate that there is every reason to persist with experiments aiming to produce a thoroughly satisfactory contrast medium for practical use in peroral cholegraphy. The risks associated with intravenous cholegraphy and Biligrafin should not be exaggerated, however. For young patients with a sound heart, Biligrafin, in spite of the blood pressure fall it causes, is not only a harmless contrast medium but also even preferable, at present, from the practical standpoint. But for patients with weak hearts and for those in the highest age groups the oral form of cholegraphy appears to be a more suitable method judging by the evidence obtained in these preliminary investigations. At present, Solu-Biloptin seems to be the contrast medium presenting the best possibilities for achieving a diagnostically satisfactory and relatively rapid examination (SALTZMAN).

In general we would emphasize, in agreement with other authors, that intravenous cholegraphy should be performed only on well defined clinical indications. Unfortunately, some confusion exists regarding the terminology for roentgen examinations of the bile-bearing organs. Reports are not infrequently found in the literature regarding cholecystographies carried out with Biligrafin; if these reports refer to examination of the gallbladder it must be said that the range of application of this contrast medium has been misunderstood. It is true that the gallbladder may often be filled with contrast medium effectively enough for diagnostic purposes, in exceptional cases even more effectively than with an oral preparation, but the peroral contrast medium produces in general better conditions for the examination of the actual gallbladder. Biligrafin should therefore be reserved for cases in which the bile ducts form the main object of investigation.

SUMMARY

Intra-arterial blood pressure measurements together with synchronous electro-cardiographic recordings were carried out in connection with intravenous cholegraphy. Peroral cholegraphy with Solu-Biloptin or Bilijodon-Natrium was also performed in 11 control cases. A fall in blood pressure was observed in all the cases in which intravenous cholegraphy was performed but not in the peroral cholegraphy cases. The risks and advantages of the two methods are discussed.

ZUSAMMENFASSUNG

In Zusammenhang mit intravenöser Cholegraphie wurden intra-arterielle Blutdruckmessungen synchron mit elektrokardiographischen Registrierungen ausgeführt. Ebenso wurde perorale Cholegraphie mit Solu-Biloptin oder Bilijodon-Natrium bei 11 Kontrollfällen durchgeführt. In allen Fällen von intravenöser Cholegraphie wurde ein Blutdrucksfall erzielt, nicht aber in denen von peroraler Cholegraphie. Das Risiko und die Vorteile der beiden Methoden werden besprochen.

RÉSUMÉ

Les auteurs ont effectué des mesures de la pression sanguine intra-artérielle et des enregistrements électrocardiographiques simultanés au cours de cholégraphies intraveineuses. Ils ont aussi pratiqué des cholégraphies par voie buccale avec Solu-Biloptin ou Bilijodon-Natrium dans 11 cas témoins. Ils ont constaté une baisse de la pression sanguine dans les cas de cholégraphie intraveineuse mais non dans les cas de cholégraphie buccale. Ils discutent les dangers ainsi que les avantages de ces deux méthodes.

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FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. KNUT LINDBLOM),
KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

CALCIUM PARA-OXY-BENSOICUM AND GLUCOSE AS ADJUVANTS IN CHOLEGRAPHY WITH BILIGRAFIN

An experimental study in the rabbit

by

JAAN NOVEK

MIZUTA (1953) increased the excretion of phenolsulphonphthalein in the bile by the injection of substances stimulating liver function. The increase was recorded in rabbits only immediately following nephrectomy and not in those examined 48 hours after the operation. MIZUTA gave '2.0 ml per kilo bodyweight of 3 % calcium para-oxy-bensoicum and 50 % glucose intravenously' 30 minutes before injecting the phenolsulphonphthalein, and found these to be the most effective of the liver-stimulating substances tested.

Since cholegraphy with Biligrafin does not always produce satisfactory contrast density the present author investigated the possibility of raising the iodine concentration in the bile by injecting calcium para-oxy-bensoicum together with glucose. The excretion of Biligrafin in the bile and urine was determined at the same time.

Technique. The technique used was briefly as follows. The animals were not deprived of water or food. After opening the duodenum, a polythylene tube was introduced into the common bile duct; the cystic duct was not ligated. When the bile flow had become stabilized, the bile was collected

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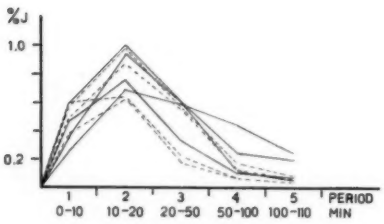

Diagram 1. Iodine concentrations in the calcium para-oxy-bensoicum series (———) and the controls (— — —). Biligrafin dose: 0.12 g per kilo bodyweight.

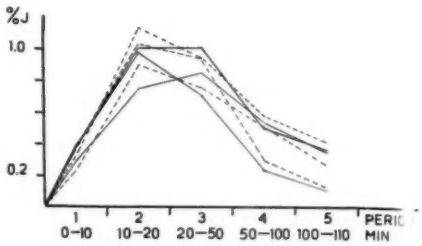

Diagram 2. Iodine concentration in the calcium para-oxy-bensoicum series (———) and the controls (— — — —). Biligrafin dose: 0.32 g per kilo bodyweight.

during a period of 10 minutes (control sample I). Calcium para-oxy-bensoicum and glucose were then injected intravenously. The bile flow during the following 10 minutes was collected as control sample II. At the end of this period, different doses of Biligrafin were injected and bile collected during standard periods of 0—10, 10—20, 20—50, 50—100, and 100—110 minutes. The urine was collected in the males with a bladder catheter, while in the females the bladder was punctured at the end of the experiment.

Calcium para-oxy-bensoicum 3 % was injected in a dose of 2 ml per kilo bodyweight and glucose 50 % in a dose of 1 ml per kilo bodyweight. When a rabbit's weight amounted to kilos and fractions of a kilo, the figure upwards to the next kilo was taken, so that the glucose could be given in whole millilitres.

Biligrafin-forte 50 % was administered in a dose of 0.12 g/kg bodyweight in 4 cases, 0.32 g/kg in 3 cases, and 0.94 g/kg in 3 cases.

The series from one of the author's earlier studies on Biligrafin (NOVEK 1959) served as controls.

Results

The highest iodine concentrations in the different calcium para-oxy-bensoicum series were as follows: a Biligrafin dose of 0.12 g/kg bodyweight produced an iodine concentration in the bile of the common bile duct of between 0.69 and 1.0 per cent (Diagram 1) and 0.32 g/kg gave between 0.85 and 1.01 per cent (Diagram 2), and 0.94 g/kg between 1.21 and 1.59 per cent (Diagram 3).

During the 10-minute period following the collection of control sample I, the calcium para-oxy-bensoicum and glucose did not raise the bile flow in any of the experiments. The injection of Biligrafin led, however, to an increase in bile flow. This increase was recorded in all the animals receiving

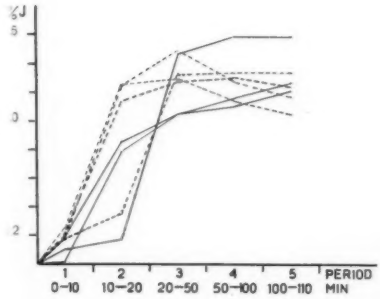

Diagram 3. Iodine concentrations in the calcium para-oxy-bensoicum series (————) and the controls (— — — —). Biligrafin dose: 0.94 g per kilo bodyweight.

doses of 0.12 g and 0.94 g Biligrafin per kilo bodyweight, while the bile flow remained unchanged in animals given 0.32 g per kilo. The increase in bile flow was not however sufficient to change the total bile volume to any noteworthy extent during the course of the experiment.

The mean excretion of Biligrafin in the common bile duct was 41 per cent of the injected quantity after a dose of 0.12 g/kg bodyweight, 34 per cent after a dose of 0.32 g/kg, and 20 per cent after a dose of 0.94 g/kg bodyweight. Four per cent, at the most, of the volume of the contrast medium injected reached the gallbladder; between 7 and 28 per cent of the Biligrafin injected was excreted in the urine.

Discussion and Conclusion

As seen from Diagrams 1 to 3, the iodine concentrations in the calcium para-oxy-bensoicum series corresponded to those in the controls when Biligrafin doses of 0.12 g, 0.32 g, and 0.94 g/kg bodyweight were given.

The bile flow (measured in millilitres per minute and kilo bodyweight) corresponded to that in the controls after the injection of 0.12 g and 0.32 g of Biligrafin per kilo bodyweight. On the other hand, a Biligrafin dose of 0.94 g/kg bodyweight led to no decrease in bile flow in the calcium para-oxy-bensoicum series. In contrast to the controls, an increase in the bile flow during the first 10-minute period following the injection of the contrast medium was noted in all three experiments; this increase was, however, too small to affect the total bile volume to any noteworthy degree.

The percentage excretion of Biligrafin in the bile was the same as in the control cases. The failure of calcium para-oxy-bensoicum and glucose to increase the excretion of Biligrafin in the bile is probably attributable to the marked hepatotropic property of the contrast medium. The liver activity provoked by the Biligrafin was apparently so lively that no further increase in the excretory capacity of the organ was possible. This agrees with MIZUTA's

experiments with calcium para-oxy-bensoicum and phenolsulphonphthalei in rabbits subjected to nephrectomy, in which he found that 'hepato-tonic could not elicit a further increase in the function of a 'hyperactive' liver.

The urinary excretion of Biligrafin was the same as in the controls.

Acknowledgements

The author wishes to express his sincere thanks to A. B. Pharmacia, Uppsala, whose financi aid and iodine analyses made the study possible.

SUMMARY

Calcium para-oxy-bensoicum was administered with glucose in a series of 10 experimenta cholegraphies in rabbits. The iodine concentration in the bile and the excretion of the contra medium in the bile and urine were found to be unaffected.

ZUSAMMENFASSUNG

Calcium para-oxy-benzoicum wurde gemeinsam mit Glukose einer Serie von 10 Kaninchen zu experimenteller Cholegraphie verabreicht. Eine Beeinflussung der Gallenkonzentration und Ausscheidung des Kontrastmittels in Galle und Urin konnte nicht festgestellt werden.

RÉSUMÉ

L'auteur a administré du para-oxy-benzoate de calcium avec du glucose au cours de cholégraphies expérimentales à une série de 10 lapins. Il n'a pas constaté de modification de la concentration de l'iode dans la bile, ni de l'excrétion du moyen de contraste dans la bile et dans l'urine.

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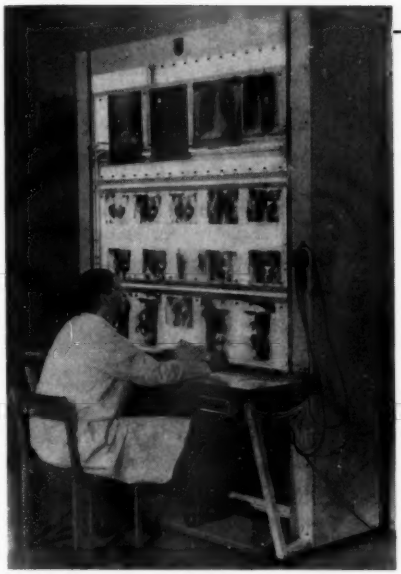

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROF. ERIK LINDGREN), SERAFIMER-LASARETTET, STOCKHOLM, SWEDEN

ENCEPHALOGRAPHIC CHANGES IN THE AXIAL PRESSURE CONE SYNDROME

by

BENGT LILIEQUIST

Intracranial expansive processes, like any other conditions causing an increase in the intracranial pressure, lead to changes in the form and volume of the brain and thereby also to discrepancies in the relationship between the size of the brain and the skull cavity. The brain lies in a closed space formed by the unyielding walls of the bones of the skull. The skull cavity is divided into three compartments by the dural folds — falx cerebri and the tentorium cerebelli. The cerebral hemispheres lie above the tentorium and are partly separated on the medial line by the falx cerebri. By forming an opening in the tentorium cerebelli, the incisura tentorii provides a communication between the supratentorial space and the posterior fossa, where the cerebellum is situated .The foramen magnum in its turn furnishes the only large opening towards the exterior of the skull cavity by connecting the posterior fossa with the spinal canal. The brain is surrounded by the liquor-filled subarachnoid spaces which, around the brain stem and over the basal surface of the brain, widen into large cavities, the cisterns. The brain is more rigidly fixed to the base of the skull by the cranial nerves, the hypophyseal stalk and the large arteries than it is to the vault where its attachments are assured only by the superficial veins running into the venous sinus.

A small cerebral volume increase, caused by a tumour or local oedema, may at first be compensated for by a corresponding compression of the subarachnoid

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space and evacuation of liquor in the vicinity of the expansive process. Whe the tumour increases in size, however, or if the oedema spreads extensively t large areas of the brain this reservoir will not suffice; more distant parts of th brain will then be displaced towards regions where space for expansion ma still be available. Such displacements can only take place either within th hemisphere affected, or laterally under the falx, or in an axial directio through the incisura tentorii or foramen magnum.

MEYER, in 1920, was the first to make a systematic investigation of changes i the shape of the brain caused by intracranial expansive processes. He describe the macroscopic appearances of different parts of the cerebrum displaced ov the edges of the dura mater and bony ridges, calling them 'herniations'. Th author also indicated the three most important sites of such dislocations: unde the falx cerebri, through the incisura tentorii or through the foramen magnun

The various types of herniations and their relation to the subarachnoid cistern were studied in a detailed investigation undertaken by SPATZ & STROESCU and by HASENJÄGER & SPATZ. These authors believed that the herniations were due to local oedema in those parts of the brain which normally constitute the walls of the cisterns. It has later been shown, however, by TÖNNIS, RIESSNER & ZÜLCH as well as by SORGO, and PERRET, in morphologic examinations of non-operated brains with tumour, and in experimental studies of artificially produced expansive processes in animals, that the herniations arise as a consequence of the mechanical displacement of parts of the brain when the total volume increases.

RIESSNER & ZÜLCH were first to correlate the different types of herniations with the actual localization of the expansive process. They succeeded in demonstrating an axial displacement downwards of cerebral parts on the medial line through the incisura tentorii, and could thus explain the occurrence of herniated tonsils due to frontal expansive processes. Further examples of an interrelationship of this kind were later furnished by ZÜLCH who pointed out that there is an axial displacement of the brain stem downwards through the incisura tentorii, particularly common in cases of frontal tumour, and herniation of the medial portions of the temporal lobe through the incisura tentorii due to pressure exerted medially and therefore more frequently met with in cases of temporal and parietal tumours.

SCHEINKER has also called attention to the axial dislocation; he coined the expression 'transtentorial herniation of the brain stem'. Displacement of the brain stem through the incisura tentorii due to supratentorial tumours had, however, been described even earlier by KERNOHAN & WOLTMAN. PERRET in an experimental study could also demonstrate the axial dislocation.

The morphologic changes in the mid-brain and pons that arise in cases of frontally situated expansive processes have recently been discussed by JOHNSON & YATES, who describe two different types of displacement, one being an axial dislocation of the brain stem downwards through the incisura tentorii, and the other a lateral deformation of the brain stem.

Temporal herniations through the incisura tentorii lead to characteristic changes demonstrable at lumbar encephalography and to some extent also at angiography, as described by AZAMBUJA, LINDGREN & SJÖGREN and by RUGGIERO. The changes appearing at encephalography are due to the fact that herniations fill up and deform the subarachnoid cisterns. Large herniations may even cause characteristic displacements of surrounding parts of the brain. Herniations into the incisura tentorii thus primarily change the appearances of the brain stem and its surrounding cisterns.

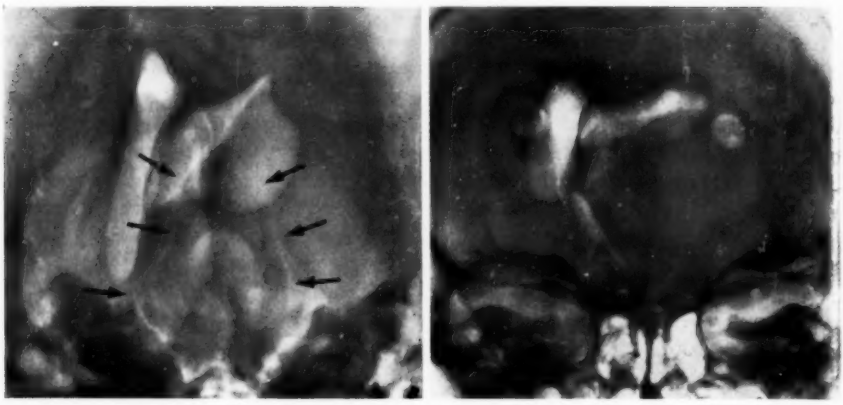
JIROUT has recently described an 'axial pressure cone syndrome', characterized by a change in the position of the medulla spinalis below the foramen magnum, which may be seen at lumbar encephalography. He states that an axial displacement of the brain stem downwards along the clivus occurs as a result of an axially directed pressure and that changes of this kind are most frequent with frontal tumours.

An indirect sign of an axial dislocation of the brain stem could earlier be registered roentgenologically by a determination of the position of the calcified pineal body. Frontal expansive processes lead to a downward and backward displacement of the pineal body, while parietal tumours cause a predominantly lateral displacement (LILJA, FRAY, VASTINE & KINNEY, LOEPP & LORENZ).

Apart from the encephalographic changes of the cisterns of the incisura tentorii caused by temporal herniations (AZAMBUJA, LINDGREN & SJÖGREN, and RUGGIERO), certain isolated observations have been made of other encephalographic changes due to frontal expansive processes (LINDGREN, and RUGGIERO), but these have not been studied in detail. They consist of (1) a typical deformation of the brain stem together with (2) an earlier unnoticed roentgenologic sign of tentorial herniation, viz. a total constriction of the aqueduct preventing the passage of air through it to the third ventricle during lumbar encephalography, and further, (3) a deformation of the third ventricle.

There have been 14 cases at Serafimerlasarettet which have been examined with lumbar encephalography and in which the air did not pass up through the aqueduct although the fourth ventricle was air-filled. Subsequently, and in all the cases, the presence of a supratentorial expansive process could be demonstrated with the aid of either ventriculography or carotid angiography. The presence of a tumour was in all the cases verified either at operation or postmortem. In ten cases the expansive process was situated in the frontal lobe; two of these were bilateral and in a further three of the cases the tumour had grown into the corpus callosum. In two cases the tumour lay in the temporal lobe and the middle fossa, respectively, in one case in the parietal lobe, and in another it had a parasagittal fronto-parietal location. As to the patho-anatomic character of the tumours, there were 2 meningiomas and 11 gliomas, of which 8 were malignant gliomas, 2 astrocytomas and 1 ependymoma. In one case, the expansive process consisted of an abscess in the frontal lobe.

In addition to the above-mentioned 14 cases, 70 cases of frontal tumour exam-



a b

Fig. 1. a) Half-axial view, supine position. The brain stem is pear-shaped but like the fourth ventricle located at the medial line. b) A.p. view. The third ventricle however is displaced laterally mainly in its superior portion.

ined by lumbar encephalography have been re-examined with special reference to the shape of the brain stem, the relationship between the aqueduct and the fourth ventricle and the deformation of the third ventricle.

I. Deformation of the brain stem

In temporal herniations the medial parts of the temporal and occipital lobes are displaced medially towards the posterior portion of the incisura tentorii, into which they are pressed down (ZÜLCH, PIA, and JOHNSON & YATES). If the herniations are bilateral the result will be that the posterior portion of the midbrain will be compressed from side to side by the herniated cerebral parts. This leads to a pear-shaped brain stem (JOHNSON & YATES). If the herniations are larger on one side, the brain stem will in addition be displaced over the medial line and it may simultaneously become deformed due to pressure from the tentorial edges on the other side (KERNOHAN & WOLTMAN, VAN GEHUCHTEN, ZÜLCH, PIA). The brain stem may also become asymmetric if the quadrigeminal plate is pressed downwards by the larger posterior herniation at the same side (AZAMBUJA, LINDGREN & SJÖGREN). A flattening of the brain stem from the side will moreover cause it to become elongated in a sagittal direction and contribute to a sagittal deformation of the mesencephalon and pons (JOHNSON & YATES).

In all the 14 cases in which the air did not pass up through the aqueduct, the brain stem had been compressed from side to side and acquired a more or les

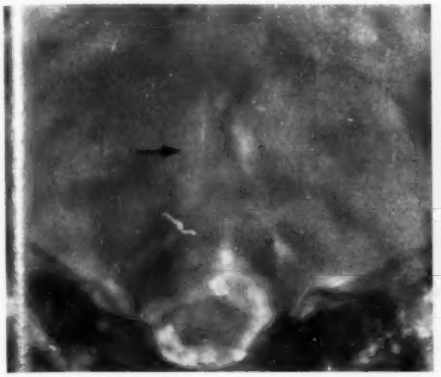


Fig. 2. The brain stem is narrow and laterally displaced.

Fig. 3. The air has been arrested in the fourth ventricle which is raised so that its distal part gives the impression of being directed upwards in relation to the clivus.

distinct pear-shape (Fig. 1a). The brain stem was narrow in four of these cases, and also more or less laterally displaced. The greatest displacement was found in the cases where the tumour was situated in the parietal lobe (Fig. 2) and in the one case with an abscess in the frontal lobe. In the other ten cases, the brain stem was not displaced over the medial line, or only very slightly so. It was generally, however, somewhat asymmetric, as in cases of postero-temporal herniations. The quadrigeminal bodies were thus located at a slightly lower level on one side than on the other indicating that the posterior temporal herniation was somewhat larger on the former side.

II. Changes in the aqueduct

The aqueduct will also be deformed as a consequence of a lateral flattening of the mesencephalon and may be transformed into a narrow slit. However, any change in the shape of the aqueduct, which normally is rounded, leads also to a reduction in its cross section, i. e. a comparative obstruction may occur. This is a fact that has been stressed by SMYTHE & HENDERSON, who performed measurements of the pressures in the lateral ventricles and in the lumbar subarachnoid space in cases of supratentorial and infratentorial tumours. They showed that in all cases with supratentorial tumour the pressure in the lateral ventricles was higher than in the lumbar canal, but that the pressures were the same if the tumour was situated infratentorially. According to these authors, the aqueduct becomes more or less compressed in cases of supratentorial tumour and they believed the constriction to arise from a temporal herniation in the incisura tentorii. PIA who arrived at similar conclusions stated that the aqueduct

is transformed into a narrow slit by deformation and displacement of the mid brain and hence that an obstruction to the passage of liquor is formed. This als leads to differences in the supratentorial and infratentorial pressures. Th deformation of the aqueduct into a narrow slit may be studied from a number o illustrations appearing in articles dealing with temporal herniations an published by different authors (SPATZ & STROESCU, HASENJÄGER & SPATZ RIESSNER & ZÜLCH, SCHEINKER, AZAMBUJA, LINDGREN & SJÖGREN, JEFFERSON PIA and PERRET).

The axial downward displacement of the mid-brain through the incisur tentorii moreover leads to a deformation of the pons, which will appear raise in relation to the clivus.

The fourth ventricle could be air-filled at lumbar encephalography in all th 14 cases included in this material but no air passed from it up through th aqueduct. A characteristic feature in 12 of the cases was that the fourth ventricl was raised and displaced backwards, giving the impression that its distal en beneath the anterior medullary velum (Vieussens' valve) was directed straigh upwards in relation to the clivus (Fig. 3). It was not obvious in the case with parietal tumour whether the fourth ventricle was raised or not. In another case, the fourth ventricle could be studied only in the p.a. view.

Except in one case (the one with parietal tumour) the passage blockage was present at the level of Vieussens' valve, i. e. immediately behind the inferior quadrigeminal bodies. The distal end of the fourth ventricle was in all the cases conspicuously broad or high which was probably due to a lateral flattening of the brain stem, analogous to the appearances seen in expansive processes in the pontine angle. The site of obstruction was thus more distal than is usual in the presence of so-called aqueduct stenoses which are always located in the aqueduct proper and at the same level as the superior part of the quadrigeminal plate where the aqueduct generally tapers off like a tube towards the obstruction. The fourth ventricle is in such cases not displaced backwards or raised, nor is the quadrigeminal plate changed or dislocated. Furthermore, the quadrigeminal cistern is not dislocated but is widened like most of the other cisterns around the brain stem. The aqueduct stenosis is as a rule associated with severe hydrocephalus which in its turn may lead to a downward herniation through the incisura tentorii. These herniations develop more slowly and moreover involve the central ganglia as well and the third ventricle together with the internal cerebral veins which are pressed downwards. A frequent encephalographic sign of this is that air is often present in the cisterna veli interpositi, which is compressed from above and like the third ventricle displaced basally.

Expansive processes in the posterior fossa (the vermis and the hemispheres of the cerebellum) also cause a change in the appearance of the mesencephalon, characterized by a kink in the aqueduct, the vertex of which is located between the superior and inferior quadrigeminal bodies (LINDGREN). The deformation of the mesencephalon in the presence of bilateral posterior temporal herniations

differs from the kinking produced by posterior fossa tumours in that the entire quadrigeminal plate is raised up and hence that the kink is now located between the third ventricle and the superior quadrigeminal bodies. A similar kink between the third ventricle and the quadrigeminal plate occurs with meningioma arising from the edge of the tentorium on the medial line but the aqueduct is then stretched and together with the quadrigeminal plate basally displaced.

The quadrigeminal cistern could be air-filled in 8 of the 14 cases. It was displaced in the same way as the fourth ventricle; thus it was displaced backwards and more or less markedly raised (Fig. 4). The cistern appeared very narrow in the lateral view and only the posterior part was air-filled. There was in these cases also a small amount of air in the subarachnoid space above Vieussens' valve. The changed appearance of the vermis was another characteristic feature; it was straight or pointed and there was an abnormal concavity at its frontal surface (Fig. 4).

Even if air passed through the aqueduct, which occurred in the 70 cases with frontal expansive processes in our material, it was found in 17 cases that the appearance of the fourth ventricle had changed and that it was distinctly raised and displaced from the clivus. The aqueduct could not be air-filled in 15 out of these 17 cases despite the presence of air in the fourth as well as in the third ventricle (Fig. 5). It is probable therefore that also in these cases there were bilateral posterior herniations which had deformed the aqueduct without however leading to a complete obstruction. Further evidence of this was provided by the fact that in 9 of the cases the brain stem in its dorsal part was considerably more narrow than usual.

III. Changes in the third ventricle

By compression of the brain stem the posterior part of the third ventricle is transformed into a narrow slit, as has previously been pointed out by JEFFERSON, SPATZ, STROESCU, and ROBERTSON. SPATZ & STROESCU could at section in several cases show that the tuber cinereum bulged down into the basal cisterns, and that at the same time the mamillary bodies were displaced backwards so that they filled out and obstructed the interpeduncular cistern.

In 4 of the 14 cases in which ventriculography had been performed as well the third ventricle could be studied. In all of them the posterior part of the third ventricle had been considerably compressed from side to side so that it had been transformed into a narrow slit. When the tumour was situated either exclusively or predominantly on one side the third ventricle was also displaced over the medial line except in one case in which there was a slight dislocation only of the ventricular system. There was thus a discrepancy between the symmetrical position of the brain stem in the incisura tentorii and the gross displacement of the superior part of the third ventricle (Fig. 1).

In one of the cases, the anterior recesses of the third ventricle were widened

Fig. 4. The quadrigeminal cistern is deformed, displaced backwards and raised in the same way as the fourth ventricle. The vermis is pointed and its anterior surface concave.

Fig. 5. Lateral view of a case in which the air passed into the lateral ventricles. The aqueduct is not air-filled despite the presence of air in the fourth as well as in the third ventricle.

and located at the entrance of the sella turcica, close to the dorsum sellae. At lumbar encephalography the air in the pontine cistern was in this case arrested against a downwards directed rounded indentation corresponding to the bulge formed by the tuber cinereum.

Similar changes in the third ventricle were found in 20 of the 70 cases of frontal tumour in which the air at lumbar encephalography passed up into the third ventricle and the lateral ventricles. The ventricle was thus constricted in its posterior portion, and in p.a. views it appeared as a narrow strip of air displaced over the medial line. In 18 of these cases it was moreover widened in its anterior part; the widening mainly involved the frontal recesses which were inflated like a balloon and located nearby the sellar entrance and the dorsum sellae. The tuber cinereum was pressed downwards into the interpeduncular cistern and the air in the pontine cistern was partly arrested below this formation. Probably the obstruction of the posterior part of the third ventricle, as well as the deformation of the brain stem and the aqueduct, could either separately or together explain the widening of the anterior part of the third ventricle.

No changes in the other cisterns of the posterior fossa occurred in any of the 14 cases with obstruction of the aqueduct, nor in any of the 70 cases of frontal expansive processes in which a herniation into the incisura tentorii could be demonstrated. There were thus neither any depression of the tonsils through the foramen magnum nor any flattening of the pontine or pontocerebellar cisterns.

Conclusions

Bilateral temporal posterior herniations associated with a downward displacement of the mid-brain and the brain stem may compress and deform the brain stem and cause it to assume a characteristic pear-shape. This may lead to a partial or complete obstruction of the aqueduct. Such changes arise most frequently with frontal expansive processes but may also occur with temporal and parietal tumours.

Similar though not so marked changes often occur in the incisura tentorii in the presence of frontal tumours, without however leading to a complete obstruction of the aqueduct.

An obstruction of the aqueduct caused by herniations due to a supratentorial expansive process may be differentiated from stenosis of the aqueduct by the fact that it has a different site. The cisterns around the brain stem are moreover as a rule widened in the presence of an aqueduct stenosis even if a displacement downwards of cerebral parts through the incisura tentorii may be observed. When on the other hand the kink in the aqueduct is due to an expansive process in the posterior fossa the pontine cistern and the pontocerebellar cisterns are always changed, and the tonsils are herniated through the foramen magnum; this is not the case when the change in the aqueduct is caused by a supratentorial expansive process.

A herniation into the incisura tentorii of the type described leads to an incomplete or complete obstruction of the aqueduct and the posterior part of the third ventricle by compression and deformation of the surrounding cerebral regions. The anterior portion of the third ventricle will consequently become widened and its recesses will bulge into the interpeduncular cistern.

SUMMARY

A characteristic shape of the brain stem, alterations in the relationship of the aqueduct to the fourth ventricle, and deformation of the third ventricle, in cases of frontal expansive processes examined by lumbar encephalography, are described and discussed with special reference to a material of 84 cases.

ZUSAMMENFASSUNG

Das charakteristische Aussehen des Hirnstammes, Veränderungen der Beziehungen zwischen Aquädukt und 4. Ventrikel und die Deformierung des 3. Ventrikels in Fällen mit frontalen expansiven Prozessen, welche mit der lumbalen Encephalographie untersucht worden sind, werden beschrieben und unter besonderer Berücksichtigung eines Materiales von 84 Fällen besprochen.

RÉSUMÉ

L'auteur décrit et étudie à partir d'une série de 84 cas une déformation caractéristique du tronc cérébral, des modifications des rapports de l'aqueduc avec le quatrième ventricule et des déformations du troisième ventricule dans des cas de lésions expansives frontales examinés par encéphalographie lombaire.

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FROM THE DEPARTMENT OF NEUROSURGERY (DIRECTOR: PROF. H. OLIVECRONA)
AND THE DEPARTMENT OF PHARMACOLOGY (DIRECTOR: PROF. B. UVNÄS),
KAROLINSKA INSTITUTET, STOCKHOLM, SWEDEN

CHANGES IN INTRACRANIAL PRESSURE DURING CAROTID ANGIOGRAPHY

An experimental investigation in cats

by

ERIK KÅGSTRÖM and PERCY LINDGREN

Changes of intracranial pressure during carotid angiography may be expected for several reasons. BROMAN and OLSSON (1948) showed that intracarotid injection of contrast media may produce disturbances in the blood-brain barrier, cerebral edema, and petechial hemorrhages in the brain. It is not unlikely that such changes will be associated with a rise of intracranial pressure.

In an earlier paper (KÅGSTRÖM, LINDGREN and TÖRNELL 1958) has also been demonstrated the marked vasodilator effect of sodium acetrizoate during cerebral angiography in cats. Injection of 0.2 to 0.4 ml sodium acetrizoate (50 per cent) into the common carotid artery in cats was usually followed by a rise in the cerebral blood flow to between two and four times the basal value — an increase which persisted for 10 to 20 minutes. When, on the other hand, corresponding amounts of sodium diatrizoate (50 per cent) were injected, they caused little or no rise. Investigations by RYDER, ESPEY, KRISTOFF and EVANS (1951), RICH, SCHEINBERG and BELLE (1953), and others, have shown that an increase in the cerebral blood flow is commonly accompanied by elevation of the cerebrospinal fluid pressure. In those studies the blood

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flow was not measured directly; changes in the flow were calculated from known or expected effects of various procedures, such as alteration of the blood pressure, inspiration of carbon dioxide, and the administration of drugs.

FOLTZ, THOMAS and WARD (1952) and BASSETT, ROGERS, CHERRY and GRUZHIT (1953) recorded the changes in the cerebrospinal fluid pressure after intracarotid injection of contrast media. FOLTZ et coll. observed, following injection of 2.5 ml and 4 ml iodopyracet (Diodrast 35 %) in cats and monkeys, an initial fall of 1 to 2 cm H_2O in that pressure; the decrease began in the course of the injection and had a duration of 10 to 20 seconds, after which there was a rise of 2 to 3 cm H_2O lasting two to three minutes. They attributed the initial fall to vasoconstriction, which they said had also been detected in the pial vessels through a Forbes' window. The ensuing rise coincided with a cortical blush and signs of dilatation of the pial vessels. Such small changes could possibly have been due to fluctuations in blood pressure, but unfortunately the authors mentioned nothing about concurrent recording of that factor. BASSETT et coll. found, after intracarotid injection of 60 to 90 ml Diodrast 50 % in dogs, a prolonged and substantial elevation of the intracranial pressure. However, the enormous doses used in their investigation limit the value of the results.

In a number of papers on complications attending cerebral angiography in human subjects (DUNSMORE, SCOVILLE and WHITCOMB 1951; ABBOTT, GAY and GOODALL 1952; KAESER and THOMAS 1954, and others) it has been observed that the incidence of such complications is apparently greatest in patients with various types of cerebrovascular disturbances. Corroborating this observation is experimental evidence presented by BROMAN, FORSSMAN and OLSSON (1950), who found that in rabbits with retarded cerebral blood flow or rabbits in which the cerebral vessels had been damaged by intra-arterial injection of 10 per cent formalin, disturbances of the blood-brain barrier followed intracarotid injection of iodopyracet 35 % in doses which had otherwise proved innocuous.

The aim of our investigation has been to elucidate the degree to which cerebral vasodilatation and any permeability disturbances that might attend cerebral angiography would cause an elevation of the intracranial pressure. These studies were chiefly concerned with one particular contrast medium, sodium acetrizoate, having a high vascular activity, although in a few experiments we used sodium diatrizoate which has a much lesser action on blood vessels.

Material and Methods

Our observations were made in experiments on ten cats weighing 2.4 to 4.2 kg and anesthetized with Dial in a dose of approximately 50 mg/kg. A tracheal cannula was inserted to facilitate respiration. A slender polythene tube was introduced retrogradely into the ligated and divided superior thyroid artery, unilaterally or bilaterally, enabling injections to be

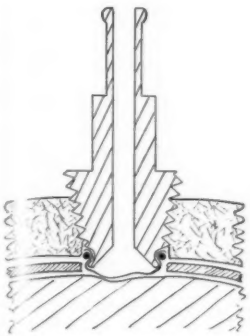

Fig. 1. Schematic representation of a 'tonometer' screwed into a trephine opening in the calvaria for recording of the intracranial pressure. The dura is opened, and to the lower end of the tonometer is attached a flaccid membrane which lies in apposition with the surface of the brain and takes up the intracranial pressure. The latter is propagated to an electromanometer via a closed, rigid, fluid-filled system.

made into the common carotid artery. The arterial blood pressure was measured with a conventional mercury manometer. In all experiments the intracranial pressure was determined by the method described below. The cerebral blood flow was also recorded in three cats by measuring the venous outflow from the superior sagittal sinus, and in one animal the pressure was measured in the superior vena cava. Blood pressure and blood flow were recorded on an ordinary kymograph, intracranial pressure and venous pressure by means of a Grass Polygraph (Model 5).

Recording of the intracranial pressure. Following sagittal division of the skin over the calvaria and removal of periosteum and muscles from one parietal region, an opening, 8 mm in diameter, was trephined. Any bleeding from the cancellous bone and from the dural margins was carefully arrested. The dura was opened by cruciform incision. A specially made hollow, threaded spindle — a type of 'tonometer' (see Fig. 1) — to the lower end of which a thin, flaccid and slightly bulging membrane had been attached, was screwed into the trephine opening so as to bring its membrane into apposition with the surface of the brain. Since this tonometer was threaded slightly conically, it could be screwed tight, the joint being quite waterproof. It was connected to an electromanometer (Statham P 23 BB) via a rigid polythene tube filled with fluid. The result was a closed system in which the intracranial pressure was propagated to the electromanometer with virtually no change in volume (12 mm^3 per 100 mm Hg). The intracranial pressure rose briefly while the tonometer was being screwed in, but had fallen again to the basal level after 5 to 10 minutes. RIECHERT and HEINES (1950) used a similar technique in human subjects; they employed a closed, air-filled system with a tonometer which communicated with the epidural space via a trephine opening. Their method did not, however, permit direct measurement of the intracranial pressure; the latter could only be estimated by observing the changes in amplitude of the dural pulsations at various pressures in the recording system. Our method, in which the dura is opened and the intracranial pressure is propagated via a membrane and a rigid, fluid-filled system, enables that pressure to be measured directly and continuously. It has proved to be very sensitive and reliable, recording even extremely small variations. Indeed, it is sufficiently precise to register those minor fluctuations of intracranial pressure that are produced by the arterial pulse wave.

The type of recording is shown in Fig. 2. In (A) and (B) the range of amplification is the same as is used in most of our experiments. The small fluctuations are due to respiratory movements. In (C) a higher amplification was used. The influence of the pulse wave is easily recorded as well as the decrease of intracranial pressure during inspiration and increase during expiration.

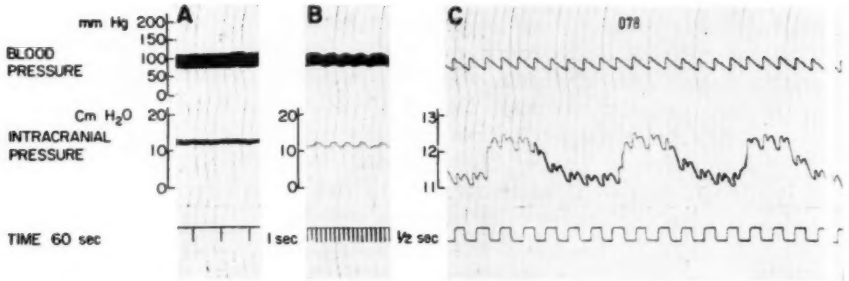

Fig. 2. Cat 2.3 kg. Dial 50 mg/kg. Recording of intracranial pressure at different amplifications and paper speeds showing the sensitivity of the technique.

Recording of the cerebral blood flow. We employed for this purpose, as in a previous investigation (KÅGSTRÖM, LINDGREN and TÖRNELL 1958), the method reported by INGVAR and SÖDERBERG (1956) for measuring the venou outflow from the superior sagittal sinus. A more detailed description will be found in the papers quoted. Briefly, the method involves removal of part of the calvaria in a groove over the superior sagittal sinus, which is incised and cannulated with a polythene tube, the blood then being conducted to a photoelectric drop recorder. It requires heparinization, which in our experiments was done with 25 mg heparin per kg administered intravenously in a 5 per cent solution.

Recording of the venous pressure. A polythene cannula filled with fluid was advanced retrogradely into the brachial vein until, according to calculations, it lay in the superior vena cava. It was then connected to a pressure transducer (Statham P 23 AA). On completion of the experiment, its position in the vena cava was checked.

Contrast media. The sodium acetrizoate used in this study was the Swedish preparation Triurol 50 % (Leo). (Sodium acetrizoate is also marketed under the proprietary names of Acétiodone, Diaginol, Rheopak, Urokon, and others.) The commercial name of sodium diatrizoate is Hypaque 50 % (Winthrop).

The contrast media were generally injected into one of the common carotid arteries in doses of 0.05, 0.10, 0.20 and 0.40 ml; occasionally both arteries were injected simultaneously. The injections were usually given at intervals of 10 to 20 minutes, though sometimes more frequently.

The internal carotid artery in the cat is very slender, and often non-functioning. The circle of Willis receives its blood chiefly from branches of the external carotid artery and from the vertebral artery. The concentration of contrast medium in the cerebral vessels after injection into the common carotid artery may therefore vary considerably from one experiment to another, a fact that must be borne in mind when the results are to be analyzed quantitatively. The relatively wide range of values obtained in an earlier investigation using the same mode of administration (KÅGSTRÖM, LINDGREN and TÖRNELL 1958) was probably due in part to these anatomical conditions.

In the present study we sought to adjust the doses so that the application times and other factors would approximate as closely as possible those in cerebral angiography in human subjects. Considering the relative body weights, 0.4 ml in a cat is roughly equivalent to 8 ml in a human being.

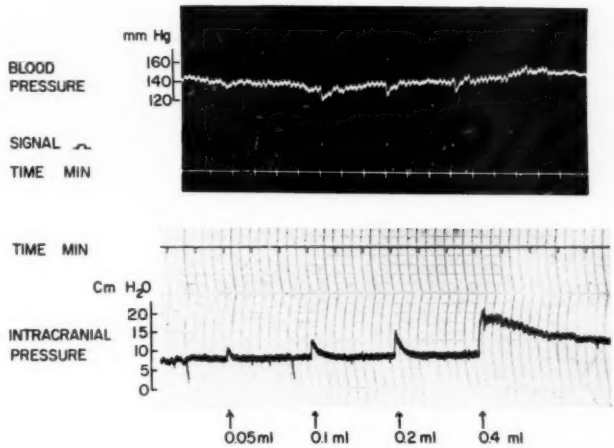

Fig. 3. Cat 2.7 kg. Dial 55 mg/kg. Elevation of intracranial pressure following injection of rising doses of sodium acetrizoate into the right common carotid artery. The injections also cause minor falls in blood pressure. (Unfortunately the blood pressure and intracranial pressure were, for technical reasons, recorded on different kymographs which did not operate at the same speed. This was also the case with the experiments shown in figs 4 and 5.)

When preparation was complete the animals were left until the blood pressure, blood flow, and intracranial pressures had become stable, before initiation of the injections. In the ten experiments a total of 63 sodium acetrizoate and 10 sodium diatrizoate injections were given.

Results

The intracranial pressures recorded at the outset of each experiment varied from 4 to 20 cm H_2O but were usually around 10 cm H_2O. Unilateral injection of 0.05 to 0.10 ml sodium acetrizoate (Triurol 50 %) into the common carotid artery produced little or no rise of intracranial pressure. After doses of 0.2 and 0.4 ml, however, there was invariably a distinct rise, which usually amounted to 10 to 15 cm H_2O (range 3 to 20 cm H_2O) above the basal level. Certain differences in magnitude of the effects were sometimes observed in single experiments when the same dose was administered repeatedly. Especially noteworthy was the frequent discrepancy in effect between injections into each of the common carotid arteries. The rise of pressure began only a few seconds after the injection and was maximal after 15 to 50 seconds. As a rule the pressure remained at that level for a minute or so, then gradually fell. Typical effects of sodium acetrizoate in increasing doses are illustrated in Fig. 3. The elevation usually coincided with a substantial, sometimes manifold increase in the pulse amplitude of the intracranial pressure.

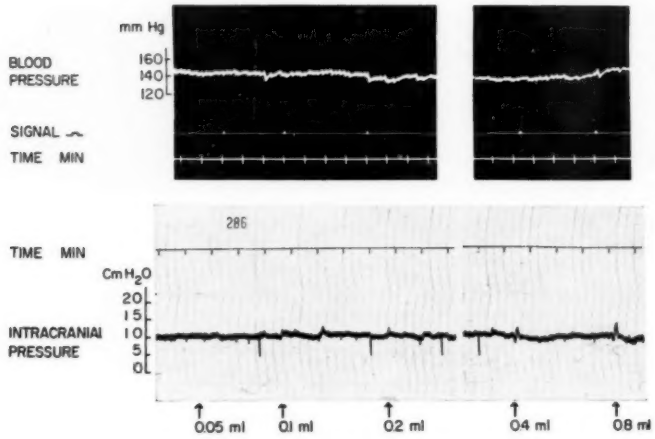

Fig. 4. Cat 2.7 kg. Dial 55 mg/kg. Recording of intracranial pressure. Effects of injection of rising doses of sodium diatrizoate into the right common carotid artery.

The duration of the rise also showed very marked individual variations. While the effect often subsided completely after only a minute or so, it sometimes took 20 to 30 minutes for the pressure to become stable, generally at the initial level. The magnitude of the rise was apparently dependent in some degree on the pre-injection pressure for greater effects were found as a rule when that pressure had been high.

Injection of sodium diatrizoate (Hypaque 50 %) into the common carotid artery in doses of up to 0.4 ml occasionally produced a very slight rise of intracranial pressure, but for the most part no change was detectable. The effects of sodium diatrizoate in mounting doses are illustrated in Fig. 4. In our earlier investigation (KÅGSTRÖM, LINDGREN and TÖRNELL 1958) on the effects of contrast media on the cerebral blood flow, we had found that sodium diatrizoate possessed very little vascular activity in comparison with sodium acetrizoate. It was not surprising therefore to find that the former agent had no major influence on the intracranial pressure. In the majority of experiments we therefore focussed our attention on the rise of pressure following the injection of sodium acetrizoate.

In view of possible summation it is worth while comparing the effects of the first and subsequent injections of sodium acetrizoate. It is then necessary to consider both the magnitude of the rise and the level at which the pressure is stabilized after the immediate effects of the injection have subsided. When the rise had ceased, the intracranial pressure did not always return to the pre-injection value; in some instances it became stable at a higher level. We

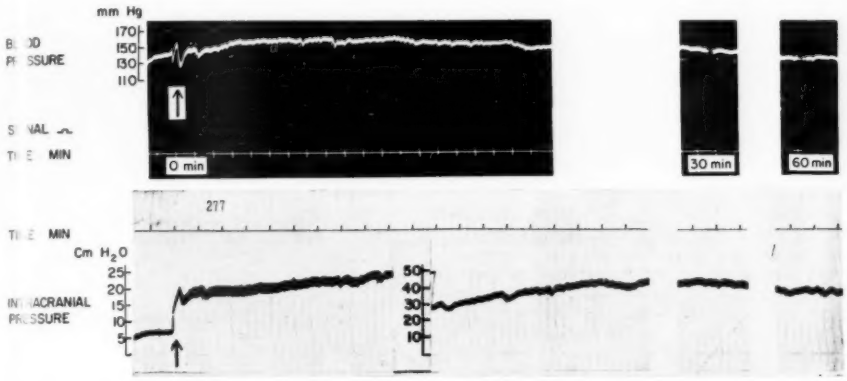

Fig. 5. Cat 3.0 kg. Dial 50 mg/kg. Simultaneous injection of 0.4 ml sodium acetrizoate (at arrow) into each of the common carotid arteries, followed by an initial rise of intracranial pressure to approximately 20 cm H_2O, then a further gradual rise to 45 cm H_2O. The pressure is still elevated (35 cm H_2O) after one hour. There is concomitant elevation of the blood pressure.

observed, however, no regular tendency toward elevation of the initial effects with repeated injections (2 to 4).

In two experiments, a prolonged, irreversible rise of intracranial pressure occurred and these require further description. In the one instance we had first given four injections of 0.4 ml sodium acetrizoate at intervals of only 2 to 4 minutes, each injection being followed by a rise to approximately 25 cm H_2O in the intracranial pressure from a basal level of around 15 cm H_2O, then a return to that level within two minutes. The pressure began to rise gradually a few minutes after the fourth injection and, after one hour, exceeded 100 cm H_2O. Subsequently it was stabilized at 80 cm H_2O. The rise coincided with an increase in blood pressure, though the latter at no time exceeded 170 mm Hg. In the other experiment we first injected 0.4 ml sodium acetrizoate unilaterally, which raised the intracranial pressure from 9 to 16 cm H_2O, with a return to normal after 13 minutes. A dose of 0.4 ml was then injected simultaneously into each of the common carotid arteries (Fig. 5); it produced an initial rise to 20 cm H_2O and a further gradual increase to 45 cm H_2O during the ensuing 20 minutes, after which the pressure fell to 35 cm H_2O and was stabilized there. A further injection of 0.4 ml bilaterally caused an immediate rise to 70 cm H_2O, and eventually the pressure became stable at 60 cm H_2O. Here too, the blood pressure rose concurrently.

Where the venous outflow was recorded concomitantly with the intracranial pressure, the durations of the rise in pressure and increase of flow were in close accord. Fig. 6 shows that the changes in pressure and flow commenced, and reached their maximums, more or less concurrently, and that the subse-

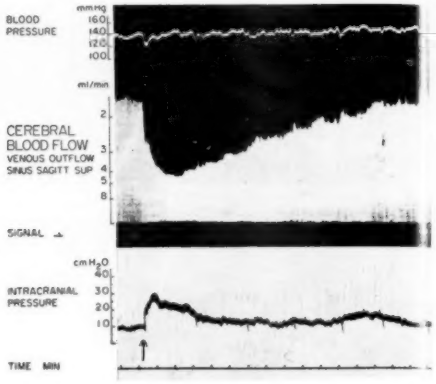

Fig. 6. Cat 3.2 kg. Dial 50 mg/kg. Simultaneous recording of blood pressure, venous outflow from sagittal sinus, and intracranial pressure. Injection of 0.2 ml sodium acetrizoate into the right common carotid artery produces an increase in flow and a rise of intracranial pressure, with close accord between the character and duration of the two responses.

quent falls were parallel. This suggests that the temporary rise of intracranial pressure following intracarotid injection of sodium acetrizoate is due essentially to cerebral vasodilatation and an increased blood volume in the brain.

The intracranial pressure is highly dependent on the venous pressure (RYDER, ESPEY, KRISTOFF and EVANS 1951). We considered it important therefore to elucidate the degree to which changes of intracranial pressure following injection of sodium acetrizoate into the carotid system might be due to an influence of the venous pressure. For this purpose we recorded the latter, in one animal, via a cannula inserted in the superior vena cava. As will be seen from Fig. 7, the rise in venous pressure elicited by raising the intrathoracic pressure (compression of the thorax) was accompanied by a parallel elevation of the intracranial pressure. Injection of sodium acetrizoate into the common carotid artery produced, on the other hand, a substantial rise of intracranial pressure with no change in venous pressure. Hence the intracranial pressure elevation which follows injection of contrast medium is a direct effect and is not due to a change in venous pressure.

Discussion

Although in this investigation we employed quantitative methods which permit the relatively accurate recording of the intracranial pressure and the blood flow in the sagittal sinus, the results must be regarded mainly as qualitative, for there are major sources of error that affect the quantitative outcome. These are touched upon in the section on methods, and have been discussed at greater length in an earlier paper (KÅGSTRÖM, LINDGREN and TÖRNELL 1958). Considering these factors, it is not surprising that we obtained

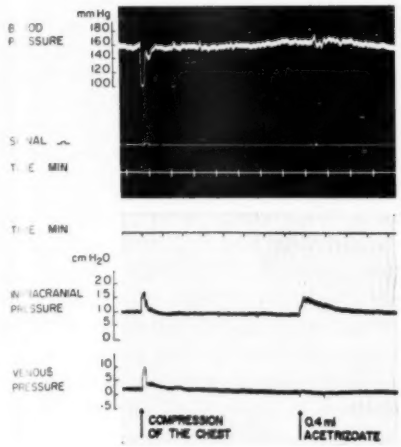

Fig. 7. Cat 3.0 kg. Dial 55 mg/kg. Simultaneous recording of blood pressure, intracranial pressure, and venous pressure (superior vena cava). Compression of the thorax produces an increase of both venous and intracranial pressures. Injection of 0.4 ml sodium acetrizoate causes a substantial rise in the intracranial pressure, with no change in the venous pressure.

a wide range of values. In view of especially the varying distribution of the amounts injected into the common carotid artery, no useful purpose would be served by comparing e. g. the dose-response behavior of different animals. We have arrived at the definite conclusion that the cat does not lend itself to quantitative studies of the effects of intra-arterially injected drugs upon intracranial functions, even though that mode of administration has been used by several previous authors (e. g. WEATHERALL 1942, FOLTZ, THOMAS and WARD 1952, INGVAR and SÖDERBERG 1957).

The changes in intracranial pressure that we observed after injection of sodium acetrizoate into the common carotid artery in doses of 0.2 to 0.4 ml, appeared to be of two different types. One of these was a swift, regular initial rise of pressure which usually amounted to 10 to 15 cm H_2O above the basal level and as a rule was reversible. To all appearances it was due to the cerebral vasodilatation which that contrast medium had been found to induce. The other type was found in only two experiments and consisted in a gradual progressive elevation of the intracranial pressure to 80 to 100 cm H_2O, commencing when the initial increase had begun to subside and reaching its maximum after 20 and 60 minutes, whereafter the pressure became stable at 60 and 80 cm H_2O respectively.

There seems little doubt that a causal relationship exists between the injection of sodium acetrizoate and the substantial, irreversible rise in pressure; but the question arises as to the mechanism behind these effects. A post-injection increase of blood flow, persisting for hours, is improbable; at all events we have not observed one. Hypoventilation associated with CO_2 retention and

cerebral vasodilatation is scarcely plausible either, since a respiratory influence was not detectable until in the final stages of our experiments and, even then, was probably secondary to the rise in pressure. No intracranial hemorrhages were found. The likeliest explanation is that severe vascular lesions occurred, with permeability disturbances and cerebral edema which produced the rise in pressure, i. e. probably a counterpart to the injuries to the blood-brain-barrier, etc. which BROMAN and OLSSON (1948) demonstrated after intra-carotid injection of various contrast media in animals. One might raise the objection, as did those authors, that the application times in clinical cerebral angiography (and in our experiments too, with the relatively small doses employed) are much shorter than those which have been associated with damage to the blood-brain-barrier in animal experiments of those authors. In a subsequent paper BROMAN, FORSSMAN and OLSSON (1950) showed, however, that certain conditions may be conducive to permeability disturbances — for example, retarded cerebral blood flow and vascular lesions in the brain — and that with repeated injections of contrast media at short intervals there may be summation of their effects.

In the two experiments wherein we observed a substantial and irreversible rise of pressure, there were in fact some circumstances which might have contributed to the development of severe vascular lesions. In one of the experiments four injections of 0.4 ml were given at intervals of only 2 to 4 minutes; in the other, 0.4 ml was injected simultaneously on each side. Yet in one or two other experiments we made repeated injections and injected contrast medium simultaneously on both sides, without obtaining an irreversible elevation of pressure. In our view, therefore, persisting elevation of pressure was due to a permeability disturbance attended by cerebral edema; but unfortunately we are unable to offer a satisfactory explanation of why this effect occurred in some animals but not in others. Further investigations on this problem are planned, however. Attention may be drawn here to the clinical observation (KAESER and THOMAS 1954, and others) that patients who show severe neurologic complications following cerebral angiography have not infrequently undergone, and subsequently undergo, a similar examination with the same technique and the same or even greater amounts of contrast medium without presenting side-effects.

There are numerous reports of reactions and complications in cerebral angiography. As regards the degree of severity, one finds all grades from mild discomfort to grave sensory and motor loss. Among the commonest side-effects are facial redness and pain in the injected half of the head, petechiae of periorbital tissues and retina, and irregularities in cardiac rhythm and respiration. Less frequent are convulsions and painful paresthesias in the contralateral half of the body, temporary or persistent palsies, loss of consciousness, and death. (For references, vide KAESER and THOMAS 1954 and BONNAL & LEGRÉ 1958.)

Such side-effects are probably attributable in great part to the contrast medium per se. Its deleterious effect in cerebral angiography may possibly be due to a toxic action on nervous structures in the brain following leakage from blood vessels, to cerebral tissue anoxia caused by temporary substitution of contrast medium for blood in the vessels, or to vascular reaction in the form of spasm, dilatation or lesions producing disturbances of permeability. It may also be due to pathologic changes secondary to these cerebrovascular disturbances, such as intracerebral hemorrhage, infarction, cerebral edema, and elevated intracranial pressure.

Many authors seem inclined to regard vasospasm as the principal cause of neurologic complications in cerebral angiography (vide e. g. CHUSID, ROBINSON and MARGULÈS-LAVERGNE 1949, DUNSMORE, SCOVILLE and WHITCOMB 1951), even though the results of animal experiments with intracarotid injection of contrast media hardly corroborate that theory (for more detailed discussion, see KÅGSTRÖM, LINDGREN and TÖRNELL 1958). There are two circumstances that may explain this discrepancy between the clinical views and the experimental findings. First, the complications may arise some considerable time after angiography, whereas observations made in animal experiments have generally referred to the time of and shortly after the injection; and secondly, the cerebrovascular disorders that are often present in patients undergoing this examination can scarcely be duplicated in laboratory animals. The majority of experimental investigations are concerned with animals having normal intracranial conditions.

In several papers (OLSSON 1950, TARLOV and ROSENBERG 1952, KAESER and THOMAS 1954), permeability disturbances are considered to be an important cause of severe complications in cerebral angiography. In the opinion of BLOOR, WRENN and MARGOLIS (1951), the histologic changes that may be found in the brain following cerebral angiography suggest that the contrast media have a selective toxic action on the vascular bed 'with (1) early vasodilatation or loss of tone, which may progress to ultimate stasis, (2) severe alterations of the permeability of the vessels, and (3) progressive cerebral edema consequent upon these changes'. If vasoparesis is the primary causative factor in post-angiographic brain lesions, it should be possible to find a correlation between the vasodilator action of a contrast medium and its ability to produce disturbances of permeability. Sodium acetrizoate has marked vasodilator properties; sodium diatrizoate, on the other hand, causes only very slight vasodilatation when injected intra-arterially. Iodopyracet seems to occupy an intermediate position (LINDGREN and TÖRNELL 1958, KÅGSTRÖM, LINDGREN and TÖRNELL 1958 and 1960). Collation of our results with those of FOLTZ, THOMAS and WARD (1952) indicates that these three substances have the same grading as regards their influence upon the intracranial pressure. WHITELEATHER and DESAUSURE (1956), using the Broman-Olsson technique in dogs, compared the deleterious actions of sodium acetrizoate, sodium diatrizoate

and iodopyracet on the permeability in the brain. The results suggest to some degree that in this respect also, acetrizoate is the most, and diatrizoate the least, harmful of the three. Since, however, some sections of the report are incomplete, no definite conclusions can be drawn. BROMAN and OLSSON (1956), in a comparative study of sodium acetrizoate (Triurol) and iodopyracet (Umbradil), found that the former was probably somewhat more toxic than the latter but that both were superior to another iodopyracet preparation, Diodrast.

OLIN (1958) recorded in a few patients the cerebrospinal fluid pressure during carotid angiography with sodium diatrizoate (Hypaque), but found that it was not appreciably affected.

The clinical significance of the changes in intracranial pressure following carotid angiography may be a matter of discussion. A rise of pressure amounting to 10 to 15 cm H_2O above the basal level, equivalent to the initial elevation produced by vasodilatation in our experiments, could hardly be dangerous in a patient with normal intracranial conditions. But if the patient due to an expansive intracranial process or some other condition has an elevated intracranial pressure with herniation of the temporal lobe, the further rise produced by injection of contrast medium may well be the decisive factor; this not least because the injection will probably have a greater influence on the intracranial pressure if the latter is already pathologically elevated at the start of the examination (cf. RYDER et coll. 1952). In consulting the literature on complications associated with cerebral angiography, it is difficult to single out any certain case wherein such a mechanism may have been present, because in communicating data in the case reports, very little attention has been paid to this possibility. TARLOV and ROSENBERG (1952) called attention, however, to the danger of complications from angiography in children with hydrocephalus.

It is naturally open to question whether the substantial effects on intracranial pressure that we sometimes found after intracarotid injection of sodium acetrizoate have counterparts in cerebral angiography in human subjects, or whether they are in some way dependent on the particular experimental conditions. Some trauma of the brain, albeit slight, is unavoidably produced with our mode of recording. In our view the results of this investigation demonstrate, at all events, the advantages of avoiding the use of contrast media with a high vascular activity for cerebral angiography in human beings.

Acknowledgement

This investigation was supported by a grant from the Swedish Medical Research Council which is gratefully acknowledged.

SUMMARY

The intracranial pressure was recorded in cats following the injection of sodium acetrizoate and sodium diatrizoate into the common carotid artery. A temporary elevation of the intracranial pressure, probably due to cerebral vasodilation, followed the injection of sodium acetrizoate; corresponding amounts of sodium diatrizoate produced little or no change. The causes of the marked effects of sodium acetrizoate and their clinical significance are discussed.

ZUSAMMENFASSUNG

Der intrakranielle Druck wurde bei Katzen nach Injektion von Natriumacetrizoat und Natriumdiatrizoat in die Art. carotis communis gemessen und aufgezeichnet. Man erhielt dabei eine temporäre Erhöhung des intrakraniellen Druckes im Anschluss an die Injektion von Natriumacetrizoat, wahrscheinlich infolge zerebraler Vasodilatation; entsprechende Gaben von Natriumdiatrizoat erzeugten nur geringe oder überhaupt keine Veränderungen. Die Fälle von deutlicher Wirkung nach Natriumacetrizoat-Gaben und ihre klinische Bedeutung werden besprochen.

RÉSUMÉ

Les auteurs ont enregistré chez des chats la pression intracranienne après injection d'acétrizoate de sodium et de diatrizoate de sodium dans l'artère carotide primitive. L'injection d'acétrizoate de sodium est suivie d'une élévation transitoire de la pression intracranienne, probablement due à une vasodilatation cérébrale; des quantités correspondantes de diatrizoate de sodium ont un effet nul ou minime. Les auteurs examinent les causes de l'effet marqué de l'acétrizoate de sodium et son importance clinique.

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FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: DOCENT B. NORDENSTRÖM), THORAXKLINIKEN, KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

SEPTAL DEFECT BETWEEN THE LEFT VENTRICLE AND THE RIGHT ATRIUM DIAGNOSED BY CARDIOANGIOGRAPHY

by

BJÖRN NORDENSTRÖM and CARL-OLOF OVENFORS

The occurrence of septal defects between the left ventricle and right atrium has been known for a long time (3, 6) and it is important for the planning of the surgical intervention to distinguish these from the usual type of ventricular septal defects. Even small defects should be operated upon since a considerable shunt may exist on account of the large pressure difference between the left ventricle and the right atrium.

The defect is situated within the small area where the left ventricle and right atrium have a common wall, that is, just cranial to the septal leaflet of the tricuspid valve in the floor of the right atrium.

We have had the opportunity to examine such a case roentgenologically. The patient, a 22-year-old woman, had had no heart symptoms but a heart murmur had been present since childhood. At mass roentgen examination the heart was found to be enlarged and auscultation disclosed a strong systolic murmur with p.m. over the 4th left costal interspace, which was considered to be due to a ventricular septal defect. The heart volume with the patient in the standing position according to JONSELL's method was 880 ml, corre-

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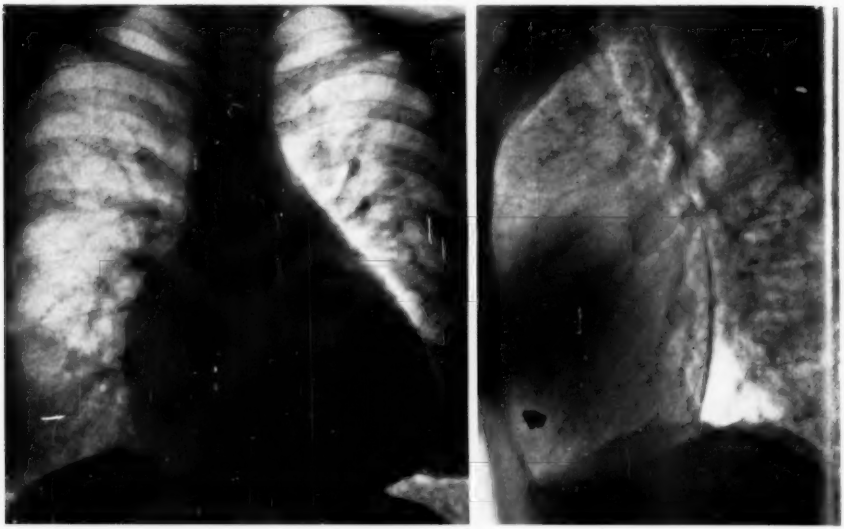

Fig. 1. Right atrium and ventricle are enlarged, and pulmonary vessels widened. A lead indicator is placed over the apex as a guide for the transthoracic puncture of the left ventricle.

sponding to a volume of 630 ml per m^2 body surface. The right atrium was chiefly enlarged, but the right ventricle and left atrium were also affected (Fig. 1). The central and peripheral branches of the pulmonary artery were considerably dilated while the aorta was of about normal width although there was perhaps some narrowing of the arch. The suggested left to right shunt could therefore very well be due to a ventricular septal defect. The right atrial dilatation was however rather against this supposition. At heart catheterisation normal pressures in the right atrium, ventricle and pulmonary artery were found. Blood gas analyses showed that arterial blood admixture occurred in the right atrium. Since it was probable that there was a shunt also between the ventricles, cardioangiography was performed with injection of contrast medium into the left ventricle after transthoracic puncture of the ventricle. Urografin 76 %, 1 ml per kg bodyweight, was injected in 2 seconds and 6 films per second were obtained in the antero-posterior and lateral projections. A high ventricular defect, measuring about 10 mm, in a craniocaudal direction, was revealed (Fig. 2). The contrast medium passed through the defect directly to the considerably enlarged right atrium before the right ventricle was filled. The defect appeared to be localized to the region of the septal leaflet of the tricuspid valve. The findings were confirmed at operation; there was, however, also a small defect in the septal leaflet of the tricuspid valve.

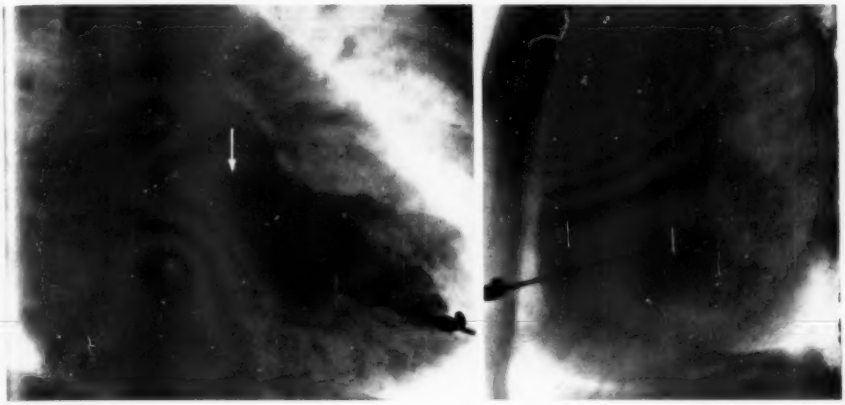

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Fig. 2. Cardioangiography with injection of contrast medium in the left ventricle. A.p. and lateral view. Arrow indicates a septal defect situated high up anteriorly through which the contrast medium is passing over from the left ventricle to the dilated right atrium.

Discussion

As far as we know, no case of defect between the left ventricle and right atrium has previously been diagnosed preoperatively. Communication between the left ventricle and the right atrium may, however, occur in a number of variants, according to the investigations made on autopsy material by PERRY, BURCHELL and EDWARDS. These authors distinguish between the following three types.

1. Besides an opening in the wall between the left ventricle and the right atrium there is a fusion of the septal tricuspid leaflet to the lower edge of the septal defect; in addition there are often small openings in the septal tricuspid leaflet. In this case the blood passes directly from the left ventricle to the right atrium.

2. A cleft or defect tricuspid leaflet lies over a high situated ventricular septal defect. In this case blood first passes from the left to the right ventricle and then regurgitates to the right atrium.

3. The third type is a combination of the two types of defects described above. The septal defect is situated both in the wall between the left ventricle and the right atrium and in the upper part of the intraventricular septum. The blood can pass from the left ventricle either to the right ventricle or to the right atrium.

The case described resembles most closely the first of these types.

A definite differential diagnosis by means of cardioangiography between groups 1, 2 and 3 still appears to be problematical. Nevertheless it seems desirable to discover preoperatively whether there is a septal defect of the first type, since it should be possible to close it from the right atrium. It seems that all three types of defects should be suspected in cases with appearances in the conventional films as described above combined with a discrepancy between auscultation findings and the blood gas analyses. In such cases the examination should be continued with cardioangiography with injection of contrast medium into the left ventricle.

SUMMARY

The first preoperatively diagnosed case of septal defect between the left ventricle and the right atrium is described.

ZUSAMMENFASSUNG

Der erste präoperativ diagnostizierte Fall eines Septumdefektes zwischen dem linken Ventrikel und dem rechten Atrium wird beschrieben.

RÉSUMÉ

Les auteurs présentent le premier cas diagnostiqué avant l'opération de communication septale entre le ventricule gauche et l'oreillette droite.

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ROM THE ROENTGENDIAGNOSTIC DEPARTMENT B (DIRECTOR: DOCENT N. P. G. EDLING), KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

A ROENTGENOLOGIC STUDY OF THE COURSE OF ULCERATIVE COLITIS

by

N. P. G. EDLING and O. EKLÖF

The frequency of a progressive course and the risk of malignant degeneration in ulcerative colitis are responsible for the current trend to surgical treatment. Colectomy or procto-colectomy has assumed far greater prominence following reports by LYONS & GARLOCK (1951), COUNSELL & DUKES (1952), CATTEL & COLCOCK (1955), ROSENQVIST et coll. (1959), and others, showing an incidence of malignant degeneration ranging from 25 to 50 per cent in patients with histories exceeding ten years. The problem of treatment is revealed in the observation of SVARTZ & ERNBERG (1949) that the majority of their ulcerative colitis patients in whom malignancy developed had long been free or almost free from symptoms and had believed that they had been cured. EDLING et coll. (1959) furthermore noted apparent roentgenologic improvement of the inflammatory lesions in a series of 26 ulcerative colitis cases with malignant changes.

With these facts in mind we studied the course of a series of cases of ulcerative colitis in order to ascertain whether the roentgen findings might be of value in the prognosis or treatment. We shall not be concerned with any correlation between the course of the condition and the treatment.

Material. The material comprises 140 of 238 cases of ulcerative colitis admitted to our hospital during the years 1940 to 1946 inclusive. In the cases surveyed the first barium enema examinations were made prior to or during

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Table 1

Distribution of cases according to the extent and the degree of changes at the initial roentgen examinatio

	Marked changes	Moderate changes	Normal findings
Terminal ileum, colon and rectum	40	0	10
Entire colon and rectum	17	3	
Distal parts of colon and rectum	5	49	
Rectum	0	9	
Atypical site (rectum not involved)	2	5	
	64	66	10

that period. Some of the patients subsequently died; the others were followed up with control barium enemas, most recently during the years 1957 to 1959. The series is confined to those cases in which the roentgenograms were available to us for examination and consists of 69 males and 71 females.

The series is part of a group of 290 cases of ulcerative colitis studied clinically by SVARTZ & ERNBERG (1949). Ten of the cases which developed malignancy are also included in the series of EDLING et coll. (1959).

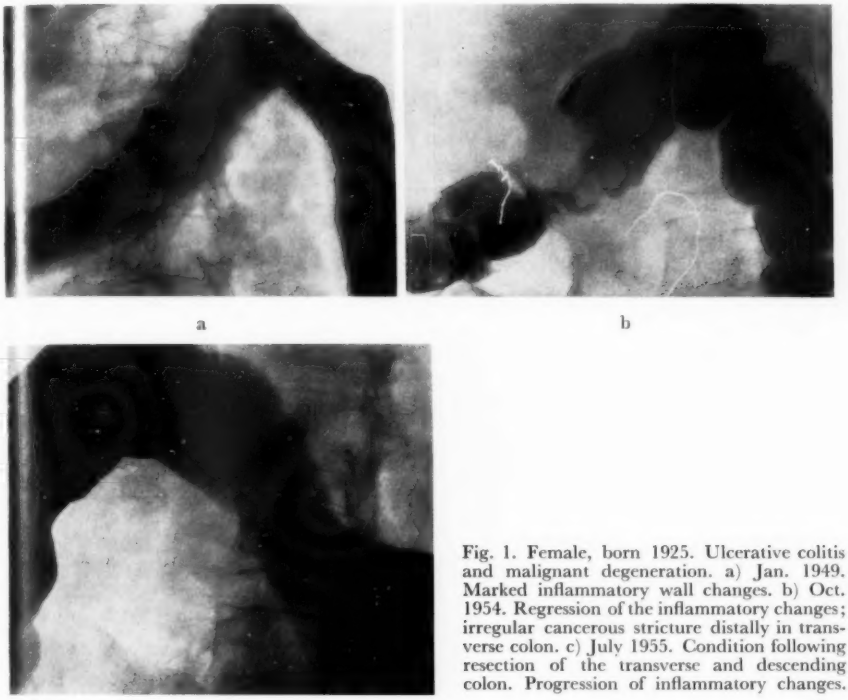
The roentgenologic examination consisted of the conventional barium enema with special views of the rectum and sigmoid colon, flexures, and ileocaecal region, as well as general views of the large intestine after filling and evacuation.

Results

We shall deal first with the initial roentgenologic findings as they apply to the extent and severity of the colitis and then concern ourselves with the roentgenologic course of the disease. Some other observations will also be considered.

The distribution of the cases with regard to the extent and degree of the condition at the initial roentgen examination is shown in Table 1. All cases with involvement of the terminal ileum in addition to the large intestine, as well as the great majority of those with involvement of the large intestine alone, exhibited marked inflammatory changes of the bowel wall. Most of the cases with lesions confined to the distal parts of the large intestine, or to the rectum alone, showed moderate wall changes. In the few cases with colitis of an atypical distribution of the lesions (rectum not involved), the changes were either marked or moderate. On the whole the extent of the inflammatory condition was commensurate with the degree of change present. The table also shows that marked and moderate changes were found in almost equal numbers of cases, and that initially ten of the cases showed no obvious roentgenologic abnormality.

The distribution of the cases according to the degree of changes and the course of disease is given in Table 2. The progressive and regressive groups comprise comparatively fairly equal numbers of cases with marked and moderate changes; the roentgenologic course in some cases showed exacerbations and



a b c

Fig. 1. Female, born 1925. Ulcerative colitis and malignant degeneration. a) Jan. 1949. Marked inflammatory wall changes. b) Oct. 1954. Regression of the inflammatory changes; irregular cancerous stricture distally in transverse colon. c) July 1955. Condition following resection of the transverse and descending colon. Progression of inflammatory changes.

Table 2

Distribution of cases according to the degree of changes and the course of the disease

Degree of changes	Regressive	Progressive	Status quo	Remainder*
Marked	26	22	5	11
Moderate	20**	31	7	8
Normal findings		1	6	3
	46	54	18	22

* Not re-examined because of death.
** Three subsequently improved and showed normal findings.

remissions but in the main a steady regression or a progression (Figs 1, 2 and 3). In the majority of cases, regression or progression was principally a change in the degree of the condition rather than in its extent. However, three of the regressive cases, each with moderate initial changes, presented normal appearances at the last follow-up examination; and only in fewer than one-third of the progressive cases did the inflammatory changes show evidence of increase.

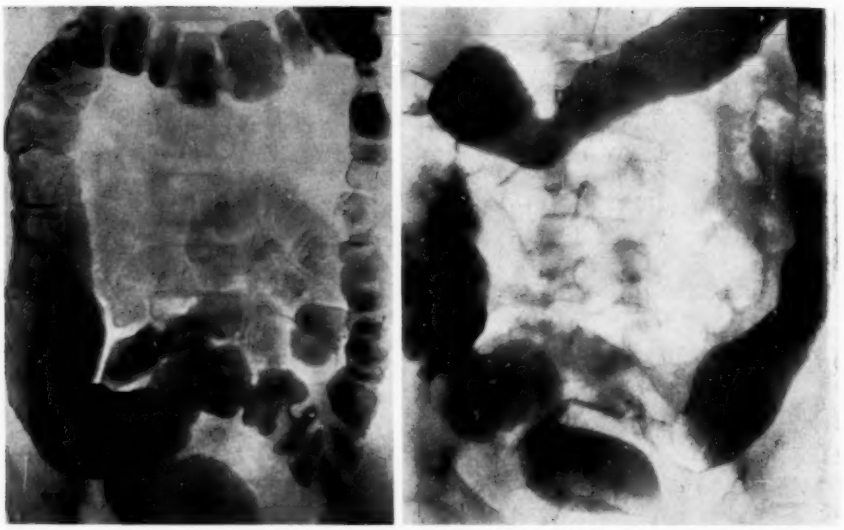


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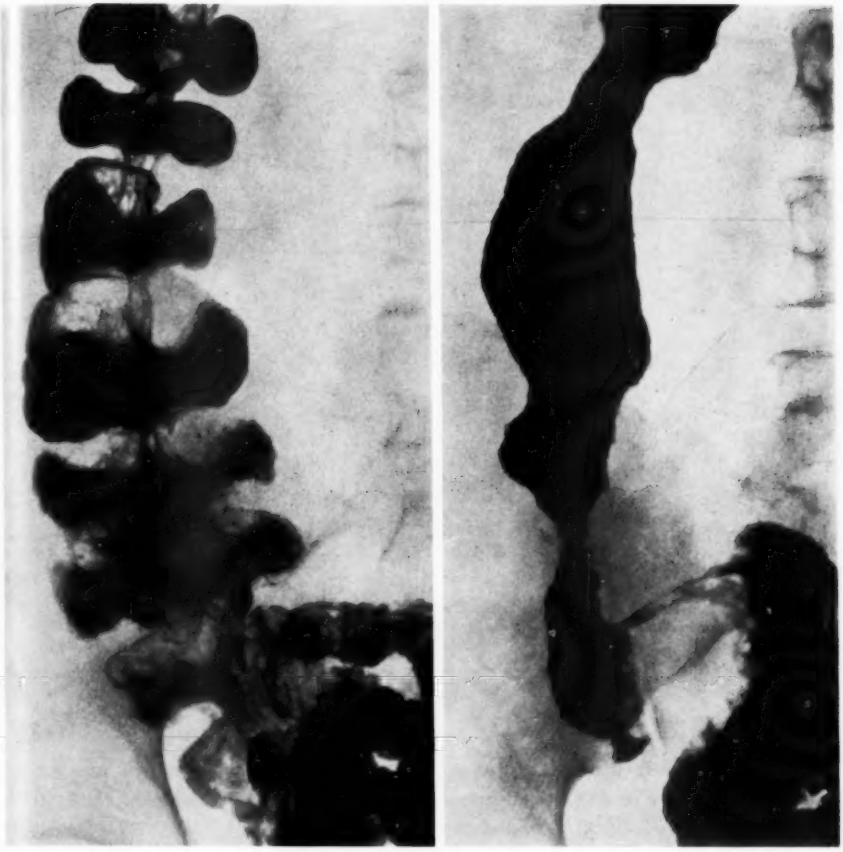
Fig. 2 a—b. Male, born 1929. Ulcerative colitis and malignant degeneration. a) Nov. 1944. Moderate inflammatory wall changes in the terminal ileum, caecum and ascending colon. b) Jan. 1951. Progression of the inflammatory changes; irregular cancerous stricture in sigmoid colon. c–d) See opposite page.

One of the initially normal cases was subsequently found to have signs of the disease. It was also noted that patients with long histories of colitis prior to the initial roentgenologic examination had a somewhat higher incidence of large intestine and terminal ileum involvement than did those with colitis of short duration. The last group in the table ('remainder') comprises those patients who died before they could be re-examined.

Nineteen of the 140 patients had malignant degeneration; fourteen died, and 5 are alive after surgical intervention. Thirteen patients died of ulcerative colitis and 19 of intercurrent disease. In one patient two tumours developed (Fig. 2). Malignant degeneration was verified either at operation or at autopsy; deaths from ulcerative colitis or intercurrent disease were confirmed by clinical or post-mortem observations, with the exception of three deaths from intercurrent disease which were recorded by private practitioners.

The extent and course of the colitis in relation to malignant degeneration and causes of death are of particular prognostic interest.

The distribution of the cases according to the extent of the colitis at the initial roentgenologic examination, the malignant degeneration, and the causes of death may be seen in Table 3. Of the 19 cases with malignant degeneration 15 showed involvement of the terminal ileum as well as of the large intestine, or an atypical distribution of the lesion; 3 presented evidence of



c d

Fig. 2 c—d. Same case as in fig. 2 a—b. c) Sept. 1954. Condition following resection of the transverse, descending and sigmoid colon and transversostomy. Regression of inflammatory changes. d) June 1959. Progression of inflammatory changes; irregular cancerous stricture in terminal ileum and caecum.

involvement of the whole of the large intestine, and 1 had changes in the distal parts of the large bowel. The incidence of deaths from ulcerative colitis, on the other hand, is evenly distributed among the groups. Cases with bowel wall changes limited to the rectum included no tumours and no deaths from ulcerative colitis. It is noteworthy that one initially negative case subsequently developed fatal colitis. The deaths from intercurrent disease included two cases of liver disease; there were also three suicides. It seemed evident that the colitis in both of the former cases was associated with the liver complications.

Table 3

Distribution of cases according to the extent of changes at the initial examination, the malignant degeneration and the causes of death

	Number of cases	Malignancy	Deaths from malignancy	Deaths from ulcerative colitis	Deaths from intercurrent disease
Terminal ileum, colon and rectum	40	13	9	3	4
Entire colon and rectum	20	3	3	3	3
Distal parts of colon and rectum	54	1	1	5	6
Rectum	9	0	0	0	2
Atypical site (rectum not involved)	7*	2**	1	1***	0
Normal findings	10	0	0	1	4
	140	19	14	13	19

* Terminal ileum involved in 3 cases.
** Terminal ileum involved in both cases.
*** Terminal ileum involved.

Table 4

Distribution of cases according to the course of disease, the malignant degeneration and the causes of death

	Number of cases	Malignancy	Deaths from malignancy	Deaths from ulcerative colitis	Deaths from intercurrent disease
Regressive	45	7	6	0	2
Progressive	55	7	4	4	3
Status quo	18	2	1	1	3
Remainder*	22	3	3	8	11
	140	19	14	13	19

* Not re-examined because of death.

The distribution of the cases according to the course of the colitis, the malignancy, and causes of death is shown in Table 4. As regards malignant degeneration there was no difference between a favourable and unfavourable course of the colitis. However, the roentgenographic appearances when the tumour was diagnosed did not necessarily coincide with the actual state of the colon at the onset of tumour growth (cf. Fig. 3). Death from colitis occurred in 4 patients with a roentgenologic progressive course and in 8 in the 'remainder' group with a clinically fulminating process.

In 29 cases, polyps and pseudopolyps were either present at the initial roentgenologic examination or developed subsequently. No distinction will be made between them, due to the difficulty in differentiating them roentgenologically. The group includes two cases of malignancy and three deaths from ulcerative colitis. The incidence of malignancy was thus lower than, and the ulcerative colitis mortality coincided with, the average in the series.

One roentgen sign in ulcerative colitis is an increase of the presacral soft tissues space. This phenomenon is discernible in true lateral views of the rectum

a b

Fig. 3. Male, born 1881. Ulcerative colitis and malignant degeneration. a) Nov. 1941. Marked inflammatory wall changes; probable incipient malignant infiltration of left side of rectum. b) June 1942. Regression of inflammatory changes; extensive irregular cancerous stricture of rectum.

Table 5

Distribution of cases according to the increase of presacral soft tissue space, the malignant degeneration and the causes of death

	Number of cases	Malignancy	Deaths from malignancy	Deaths from ulcerative colitis	Deaths from intercurrent disease
Moderate increase	25	2	2	4	2
Marked increase	13	2	2	2	4
	38	4	4	6	6

and sacrum (Fig. 4) and occurred in 38 cases. A soft-tissue thickness of 1 to 2 cm was regarded as a moderate increase, while more than 2 cm was considered a marked increase. The distribution of the cases with respect to an increase in the presacral soft tissue space, the malignant degeneration and causes of death is shown in Table 5. The incidence of malignancy is on a par with, and the ulcerative colitis mortality higher than, the average in the series. It may be noted that these cases include almost half the number of deaths in ulcerative colitis. Definite conclusions would, however, require the investigation of a larger series.

Fig. 4. Female, born 1887. Ulcerative colitis. Marked inflammatory wall changes; considerable increase of presacral soft tissue space.

The distribution of the tumours in the colon and rectum is illustrated in Fig. 5. Twenty tumours are recorded, including two in a single case (P_1 and P_2). A quarter of the tumours were located in the rectum and lower part of the sigmoid colon, and three quarters more proximally in the colon. In the case with two tumours, one was situated in the lower part of the sigmoid colon and the other in the caecum and ascending colon where inflammatory lesions had been noted at the initial roentgen examination (cf. Fig. 2).

In most of the cases, the infiltration was well defined in the films (cf. Figs 1, 2b and 3), but in some cases contiguous lesions in the bowel wall made any attempt at diagnosis difficult (cf. Fig. 2d). Microscopically, eighteen of the tumours were adenocarcinomas with greatly varying degrees of differentiation, and two were sarcomas. Five of the carcinomas were observed to be colloid secreting; this phenomenon was not noted in the remaining cases.

Though not essentially a radiologic consideration, the age at onset and the duration of the colitis will be discussed in relation to some of the radiologic findings.

The distribution according to the age at onset and to the extent and severity of the disease revealed that the cases with early onsets developed more extensive and severe lesions than did those with late onsets. The earlier the onset the more marked were the subsequent changes. The incidence of normal radiologic findings was highest in the cases of late onset.

The distribution with respect to the age at onset, malignancy, and average duration of colitis is shown in Table 6. Nearly half the amount of tumours were in patients who were under 15 years of age at the onset of colitis though those patients constituted only one-fifth of the series; of the patients with onset of colitis prior to the age of 30, fewer than two-thirds had the great majority of the tumours. It will be noticed that the average duration of colitis was

Table 6

Distribution of cases according to the age at onset, the malignant degeneration and the average duration of colitis

	Total number of cases	Average duration of colitis, years	Number of cases with malignancy	Deaths from malignancy	Average duration of colitis, years*
Onset before age 15	27	16.6	8	7	16.5
Onset at age 15 or later	113	18.0	11	7	16.3
Onset before age 30	85	18.7	17	12	17.0
Onset at age 30 or later	55	16.1	2	2	11.5

* Up to diagnosis of tumour

Table 7

Distribution of cases according to the duration of the disease, the malignant degeneration and the causes of death

Duration in years	Number of cases	Malignancy	Deaths from malignancy	Deaths from ulcerative colitis	Deaths from intercurrent disease
0— 5	140	1	1	4	4
6—10	131	2	1	2	5
11—15	121	4	4	2	4
16—20	97	8	6	3	3
21—25	44	3	2	2	1
26—30	14	1	0	0	0
31—35	4	0	0	0	1
36—40	2	0	0	0	1

approximately the same in the various groups. The ulcerative colitis mortality was more evenly distributed in the age groups. Also of interest is the fact that the age at onset of the colitis averaged 27.2 years in the entire series and 20 years in the nineteen tumour cases. The average duration of colitis in the total series was 17.7 years, and in the nineteen tumour cases prior to diagnosis 16.4 years. It may also be noted that the last two tumour cases represented in Table 6 had onset ages of 38 and 53 years, respectively, and that the tumours were localized to the rectum.

The distribution according to the duration of disease, the malignant degeneration, and causes of death is given in Table 7. The number of cases is too small for an accurate determination of the incidence of malignancy in the various duration groups. Malignancy does appear to be commoner, nevertheless, in the groups with longer durations. The figures do not, however, indicate that a long duration in itself is a prerequisite for tumour development. The deaths in ulcerative colitis are more evenly distributed.

Discussion and Conclusions

The roentgenologic demonstration of bowel wall changes in ulcerative colitis is an important factor in the diagnosis and subsequent study of the

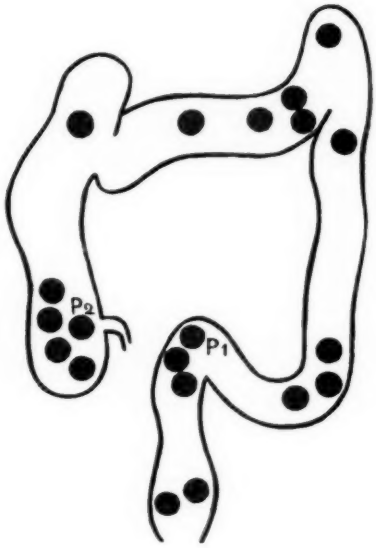


Fig. 5. Ulcerative colitis and malignant degeneration. Distribution of 20 tumours. P_1 and P_2 depict the same patient as in fig. 2.

course. BACON (1958), as surgeon, stated that roentgenologic examinations are invaluable and should be made in all cases. ALM & IHRE (1958), as physicians, advocated regular barium enema follow-up examination at least once a year. The insidious course of ulcerative colitis and the exceptional virulence of an associated malignant growth make it difficult to plan treatment, especially as the patients often feel well in spite of marked and extensive changes in the colon. It is therefore essential for the patient's welfare that the physician, surgeon and roentgenologist confer on the treatment and the times for roentgenologic follow-up examinations.

Certain facts have emerged in the present material which may be of value as regards prognosis and treatment.

The extent of the bowel wall changes was commensurate, on the whole, with the degree of the changes. Marked and moderate changes were recorded in approximately equal numbers in regressive and progressive cases, except in those with a purely rectal involvement where the course was invariably mild. The latter observation concerning the rectum is in accord with the clinical views of MONAGHAN (1944) and ALM & IHRE (1958). In the great majority of cases the extent of the inflammatory process remained unchanged (HERN 1931, RICKETTS et coll. 1948, WARREN & SOMMERS 1949, SLOAN et coll. 1950). However, only in fewer than one-third of the progressive cases did the changes in the colon wall extend upwards from the region where they were initially observed to cease; in a very few cases with regressive courses, moreover, the

involved area decreased. Most deaths from ulcerative colitis occurred in the roentgenologically progressive and clinically fulminating cases.

The incidence of malignancy was greatest in cases of early onset and those in which the inflammatory lesions were marked and involved the terminal ileum as well as the large bowel (JACKMAN et coll. 1940, KASICH et coll. 1949). The incidence of malignancy was not correlated to either regression or progression of the colitis.

The oncogenetic significance of polyps and pseudopolyps in ulcerative colitis is discussed in the literature (COFFEY & BARGEN 1939, BACON 1958). In our material, however, the presence of polyps and pseudopolyps influenced neither the prognosis of the colitis nor the malignant degeneration.

Cases with an increase in the presacral soft tissues had a higher colitis mortality than the average in the material, though not a higher incidence of malignancy.

To sum up, as regards the course of the ulcerative colitis itself, the findings at the initial roentgenologic examinations provide no true guidance, but follow-up examinations showed a poorer prognosis for the progressive than for the regressive cases. As regards malignancy, on the other hand, marked and extensive initial lesions may develop into graver conditions than do moderate lesions, but the outcome could not be predicted from the course of the inflammatory process.

The incidence of malignancy in ulcerative colitis varies greatly in the literature. The incidence in surgical series ranges from 9 per cent (WECKESSER & CHINN 1953) to 50 per cent (CATTEL & COLCOCK 1955), and in medical series from 0 per cent (FELSEN & WOLARSKY 1949) to 18.1 per cent (WHELOCK & WARREN 1955). The discrepancies stem from varying methods of selection and analysis of material and differing durations of follow-up periods. The protracted course of ulcerative colitis is usually cited as a prime factor in malignant transformation. Our series is not yet ready for a definite analysis of this question. It would appear, however, from our results that early onset of the disease and marked and extensive bowel wall lesions are more decisive factors in tumour development than is the duration itself.

A quarter of the tumours were located in the rectum and lower part of the sigmoid colon, and three quarters at higher levels (WHELOCK & WARREN 1955, EDLING et coll. 1959). As opposed to this, general experience shows that 60 to 70 per cent of ordinary colonic tumours are situated in the rectum and lower part of the sigmoid colon. This difference in localization has not yet been satisfactorily explained. However, in our series the age at the diagnosis of the tumour averaged 36 years whereas in general it is 60 to 64 years (HULTBORN 1952, SLANEY & BROOKE 1959). It therefore seems to us that age is an important factor in the localization of the malignant processes. Viewed in this way, the situation of tumours in ulcerative colitis may be more readily understood. This will not be the case, however, if duration is taken as the main predisposing factor in malignant transformation. Since the distal parts of the

colon as well as the rectum are involved in the great majority of cases, and since the inflammatory changes, according to a widely held opinion, tend to start in them, they should also be the most likely sites for tumour development.

The relatively low age of the patients who develop malignancy in ulcerative colitis probably accounts also for the virulence of the tumour growth.

The roentgenologic examination is of greater importance in the diagnosis of malignancy associated with ulcerative colitis than in that of ordinary colonic tumours which in most cases can be revealed at procto-sigmoidoscopy.

There has been some discussion concerning the relationship of malignant degeneration to ulcerative colitis. In our series malignancy occurred at much earlier ages and at quite different sites than those associated with ordinary colonic tumours. These facts point to a definite relationship.

As regards technique, it should be mentioned that the absence of retrograde filling of the terminal ileum in a barium enema examination unconditionally calls for a barium meal and examination of the ileocaecal valve and terminal ileum.

SUMMARY

The authors investigated the course of ulcerative colitis in a material of 140 cases to ascertain the value of the roentgenologic findings in the prognosis and treatment. The roentgenologic findings are correlated to the age of the patient at onset and to the duration of the colitis. The relationship between ulcerative colitis and malignant degeneration is discussed with special reference to the age factor.

ZUSAMMENFASSUNG

Die Autoren untersuchten an einem Material von 140 Fällen den Verlauf von Colitis ulcerosa um den Wert der Röntgenbefunde bezüglich Prognose und Behandlung zu untersuchen. Die Röntgenbefunde werden mit dem Alter des Patienten beim Krankheitsbeginn und der Dauer der Colitis korreliert. Die Beziehungen zwischen Colitis ulcerosa und maligner Degeneration wird mit besonderer Rücksicht auf den Altersfaktor diskutiert.

RÉSUMÉ

Les auteurs ont étudié l'évolution de la colite ulcéreuse sur une série de 140 cas pour juger la valeur des signes radiologiques pour le pronostic et le traitement. Ils recherchent une corrélation entre les signes radiologiques d'une part, et l'âge du malade au début de la maladie et la durée de la colite d'autre part. Les auteurs examinent les rapports entre la colite ulcéreuse et la dégénérescence maligne, en particulier en fonction de l'âge.

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FROM THE INSTITUTE OF RADIOPHYSICS (DIRECTOR: PROF. ROLF M. SIEVERT), KING GUSTAV V JUBILEE CLINIC, KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

IRON-ORE CONCRETE IN RADIATION PROTECTION

by

R. THORAEUS

In most recommendations of materials for protection against high energy radiation ordinary concrete holds a paramount position from the standpoint of economy, efficiency, and structural adaptability. This is clearly justified by its properties. The volume weight (density) is 2.0 to 2.2 g/cm³, which can be raised to about 2.4 by vibrating the material after it has been poured into the moulds, and with ingredients in suitable proportions the material shows strength properties which make it suitable for building construction purposes. The only disadvantage is the comparatively large thicknesses required for radiations of high energy.

Iron-ore concrete was introduced as a radiation protection material by SIEVERT (4) as early as 1933. It was intended at that time for protection barriers against radium gamma radiation. The employment of the readily available high grade Swedish iron ore as an aggregate produced a concrete the density of which was 3.7 g/cm³; its strength was found to be about the same as that of ordinary concrete. Being both convenient and space saving, the new material could be used for both protection and building construction. As far as we know it was first used in this connection in 1935, when the telegamma therapy section in the basement of the present building of the Radiumhemmet was constructed.

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The use of iron-ore concrete for protection barriers against gamma radiation from the new kilocurie Co-60 therapy unit at the Radiumhemmet was described in a recent book (1). The modern vibration method was employed, resulting in an increase of the density to 3.8 g/cm³, and of the strength to somewhat above that of ordinary concrete. This material made it possible to reduce the thickness required for adequate protection by about 40 per cent in comparison with ordinary concrete; such a means of saving space is of considerable value when the area available for the installation is limited.

In the preparation of iron-ore concretes it is important that the basic materials are carefully selected and properly mixed in the right proportions. The essential factors are briefly discussed in the following, collected from the experience gained over the last few years, and particularly from tests carried out in 1957 on a number of 20 cm cubes of both vibrated and unvibrated iron-ore concretes.

A satisfactory material can be produced only if two conditions are satisfied. The first is that high-grade iron-ore aggregates are used in two different grain sizes, one of maximum 3 mm, corresponding to ordinary sand, and the other of maximum 80 mm, corresponding to stones or 'chippings'. The second condition is a suitable water-cement ratio; this ratio is given in litres of water per kilogram of dry cement. The water-cement ratio is of particular importance for both the strength of the material and its resistance to water. The composition is given below (according to figures obtained from Mr H. Hagskog, the construction engineer of our hospital):

1 kg cement;
4.4 kg iron-ore 'sand', grain size max. 3 mm;
8.2 kg iron-ore 'chippings', grain size max. 80 mm;
Water-cement ratio = 0.57.

As already mentioned, iron-ore concrete may be vibrated in the same way as ordinary concrete. By this mechanical treatment of the material, immediately after it has been poured into the moulds, air bubbles are effectively removed, and the moulds become completely filled. This results in a considerable increase in density. In an official Swedish investigation in 1957 of 20 cm cubes it was found that the density of the unvibrated iron-ore concrete was 3.4 g/cm³, and that of the vibrated material 3.8 g/cm³, i. e. an increase in the density of about 12 per cent. The vibrated iron-ore concrete was thus deemed suitable for the purpose in question.

The strength of vibrated iron-ore concrete is the same as, or somewhat higher than ordinary concrete. It may be reinforced with iron rods to the extent required, and has thus proved to be an excellent material for building construction purposes. Its protective power against high energy radiation will now be considered.

We may say that in general the purpose of all forms of radiation protection

is to prevent the exposure of individuals to radiation levels higher than th maximum permissible. If we consider a certain source of radiation for tel therapy, this should be surrounded by an adequate housing in which there is collimating aperture and a device to turn the beam 'on' and 'off'. It appea from the NBS recommendations (3) that the housing and collimating devic should be so constructed that at one metre in any direction from the sourc with the useful beam 'off', the maximum dose rate should not exceed 10 mr/h and the average dose rate should not exceed 2 mr/hr. Furthermore, the leakag radiation through the shielding and collimating devices when the beam 'on' should not exceed one per cent of the useful beam at one metre from th source.

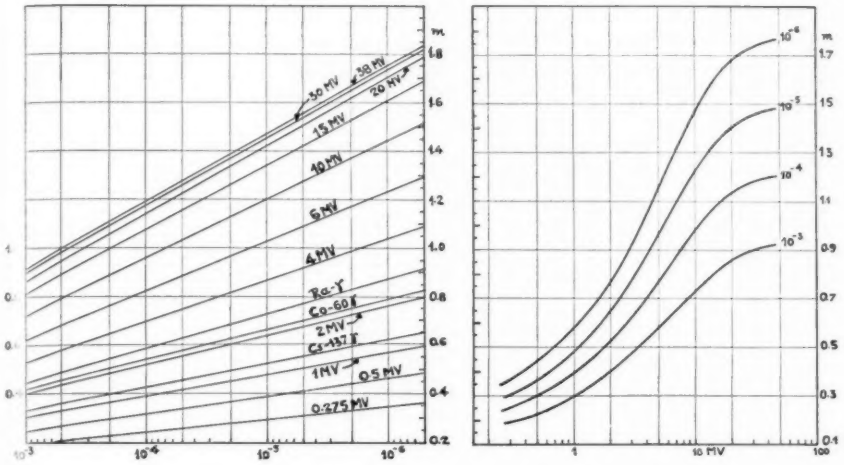
The protective barriers surrounding the treatment room should afford th required protection to individuals in the adjacent rooms. The barriers thu function as interposed attenuators to produce sufficient reduction in the usefu beam, the leakage radiation, and the scattered radiation. If they are of dimensions adequate for the useful beam, they will also be sufficient for any leakag and scattered radiation. If protective barriers sufficient for the primary roentgen radiation from a betatron are provided in all directions, no specific consideration need be given to shielding against the electron beams from the same unit.

In most radiotherapy installations personnel are not usually located closer than 50 cm to the protective barrier. Individuals in adjacent rooms should not receive more than 0.1 roentgen per week; from this condition it is easy to compute the requisite attenuation factor of the barrier. For the final determination of the barrier thickness, knowledge of the attenuation as a function of the thickness for the radiation in question is required.

An investigation by WYCKOFF and KENNEDY (6) shows that the attenuation of radium gamma radiation is very nearly the same in ordinary concrete as in steel, if the materials are compared on the basis of grams per square centimetre. The broad beam attenuation curves given by them are stated to be applicable over the range of atomic numbers between those of steel and concrete, provided the same mass of barrier is used. This has been verified by comparison of experimental results for iron with those for concrete. In a later paper by KENNEDY, WYCKOFF and SNYDER (2) the same result was obtained for cobalt 60 gamma radiation.

From these observations and by combining the experimental results in some of the quoted papers (2, 3, 6, 7) it has been possible to collect the information required to obtain a survey of the attenuation of various radiations in iron-ore concrete (Fig. 1). It will be seen that it is easy to find the thickness of iron-ore concrete required to obtain the attenuation calculated, or wanted for other reasons, for the radiation in question.

In the book already mentioned (1), WALSTAM has given the result of an attenuation measurement of the cobalt 60 gamma radiation in iron-ore con-



Figs 1 and 2. Thickness (in metres) of iron-ore concrete required to obtain a given attenuation factor at various radiations (left diagram) and, respectively, the attenuation factors 10^{-3}, 10^{-4}, 10^{-5}, 10^{-6} as a function of the maximum energy of roentgen radiation (right diagram).

crete. It may be of interest to compare his results with that given by the Co-60 curve in Fig. 1.

He found the attenuation factor of iron-ore concrete, 80 cm thick, to be about 1×10^{-6}; from Fig. 1 a value of 8×10^{-7} is obtained. Taking into consideration the fact that WALSTAM himself estimates his measurement result to be inaccurate within $\pm$ 20 per cent, because of some uncertainties and the low dose rates to be measured, we may say that the agreement is sufficient for the purpose in question.

In Fig. 2 the thickness of an iron-ore concrete barrier is shown as a function of the peak energy of the roentgen radiation for the attenuation factors 10^{-3}, 10^{-4}, 10^{-5} and 10^{-6}. It appears that the required change in the thickness is greatest over the region 1 to 10 MV. Above 10 MV the required change decreases, and from about 40 MV upwards the necessary thickness remains nearly constant. This agrees well with the NBS Handbook 55, according to which the 38 MV curve can be used as approximately correct up to 100 MV. The type of diagrammatic presentation used in Figs 1 and 2 is probably more convenient to the reader than any of those commonly used elsewhere.

In a previous paper (5) the author has compared extensive series of measurements of narrow and broad beam attenuations in lead. In that connection the term 'broad beam factor' was introduced and specified to be the factor by which the thickness obtained from the narrow beam attenuation should be multi-

Table 1

Values of broad beam factor to be expected for iron-ore concrete

Radiation	HVL in mm of radiation	Attenuation factor	Narrow beam thickness cm	Broad beam thickness cm	Broad beam factor Individua	Broad beam factor Average
0.257 MV roentgen	3 Cu	10^{-6}	41.5	57.3	1.33	
		10^{-5}	34.5	48.3	1.40	1.40
		10^{-4}	28	39.5	1.41	
0.5 MV roentgen	5.5 Cu	10^{-6}	52	66.5	1.28	
		10^{-5}	49	63	1.28	1.28
1 MV roentgen	9 Cu	10^{-5}	67	82.5	1.23	
		10^{-5}	63	78.5	1.24	1.24
1.4 MV roentgen	11 Cu	10^{-6}	81	89	1.10	
		10^{-5}	76	84.5	1.11	1.11
		10^{-4}	60	68	1.13	
Co-60 gamma	14.5 Cu	10^{-6}	95	119	1.25	
		10^{-5}	90	112	1.25	1.26
		10^{-4}	72	91	1.26	
		10^{-3}	54	68	1.26	
Ra gamma	13.3 Cu	10^{-6}	108	126	1.17	
		10^{-5}	101	118	1.17	1.19
		10^{-4}	78	95	1.22	

plied in order to obtain the thickness which would give the same numerical value for the broad beam attenuation.

A study of the broad beam factor for various radiations in concrete of 2.35 g/cm³ density has been made from the experimental results given in the papers quoted. The thicknesses were recalculated to correspond to a density of 3.8, and the results obtained are collected in Table 1. In the diagram shown in Fig. 3 the factors are plotted against the HVL in mm of copper of the radiations. As appears from Table 1 the broad beam factor does not change considerably with the thickness. It thus seems reasonable to expect that the broad beam factor of iron-ore concrete is about the same.

The 'equivalence' between mono-energetic radiation and roentgen radiation, the latter being a range of energy components, or a so-called 'bremsstrahlung', is sometimes considered, and then usually referred to penetration. It is evident that no real equivalence exists, but nevertheless such a comparison

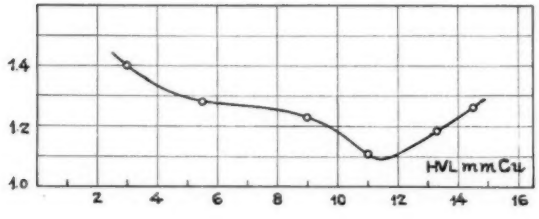


Fig. 3. Computed broad beam factor of iron-ore concrete as a function of the HVL in mm of copper of the radiation.

Table 2

Thickness of iron-ore concrete to obtain given broad beam attenuation factors

Attenuation factor	Cs^{137} gamma	1.4 MV roentgen	Co-60 gamma	2.4 MV roentgen
10^{-3}	35 cm	33 cm	42 cm	42 cm
10^{-4}	43 »	43 »	54 »	55 »
10^{-5}	53 »	52 »	67 »	68 »
10^{-6}	63 »	62 »	79 »	81 »

nay be of interest, and may also be permitted, provided that no particular conclusions are drawn from the results.

From curves similar to those in Fig. 2 it has been possible to study the attenuation in iron-ore concrete of the mono-energetic gamma radiation of Cs 137 and the very nearly mono-energetic gamma radiation of Co 60 (1.25 MV as the average of 1.17 and 1.33 MV) with that of roentgen radiation of various peak energies. The result is shown in Table 2. In this region of attenuation, 10^{-3} to 10^{-6}, which is of direct interest in radiation protection work, the result shows that the Cs 137 gamma radiation has very nearly the same penetration as the 1.4 MV roentgen radiation. As far as attenuation is concerned they may thus be considered 'equivalent' in the region investigated. The relation between Co 60 gamma radiation and 2.4 MV roentgen radiation is essentially the same.

From the results presented above it may be concluded that the present experience of iron-ore concrete in radiation protection technique has confirmed SIEVERT's opinion and shown that it is really an excellent material for protection barriers against high energy radiation. It is, however, also rather expensive, the cost per unit mass offering the same attenuation being between two and three times as high as that of ordinary concrete (both materials specified as vibrated and ignoring any saving in area and construction costs). If all considerations are taken into account, the difference might probably be reduced. A final result, however, can only be obtained from a comparison of the alternatives of the expert employment of the materials in a specified case. The weight of the protective barriers is the same for both the materials, which means the same strength requirements for supporting walls, floors, etc. The use of iron-ore concrete will probably be somewhat limited. It will, however, always be of a particular value in cases where existing protection barriers need to be reinforced and it is essential that there shall be the smallest possible loss in space.

SUMMARY

The use of iron-ore concrete for the production of protective barriers against high energy radiation is described. The ingredients and composition are specified and the conditions for the production of a high grade material are discussed. The protective power of the material is studied on the basis of the attenuation properties and the broad beam factor.

ZUSAMMENFASSUNG

Die Verwendung von Eisen-Erz Beton für die Herstellung eines Schutzes gegen Strahlu hoher Energie wird beschrieben. Die Bestandteile und Zusammensetzung werden angegeb und die Bedingungen für die Erzeugung eines hochwertigen Materials besprochen. D Schutzwirkung des Materials wird auf Grund der abschwächenden Eigenschaften und d Breitstrahlenfaktors studiert.

RÉSUMÉ

L'auteur décrit l'utilisation du béton au mineral de fer pour construire des murs de pr tection contre les radiations de haute énergie. Il indique les ingrédients et la composition c ce béton et étudie les conditions permettant de produire un matériau de très bonne qualit Il étudie le pouvoir protecteur de ce matériau en tenant compte de ses propriétés d'atténu tion et du facteur de largeur du faisceau.

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